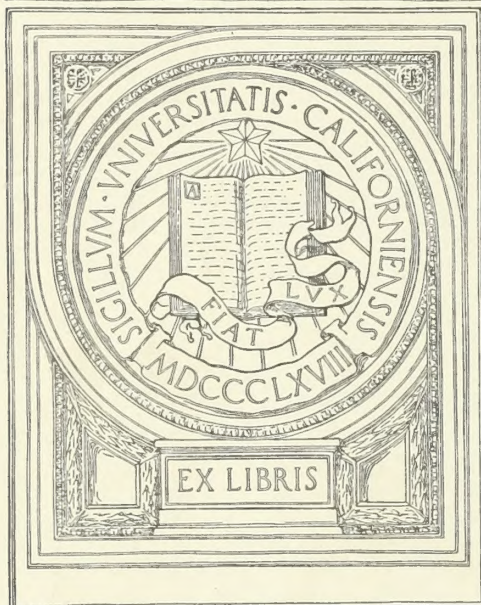




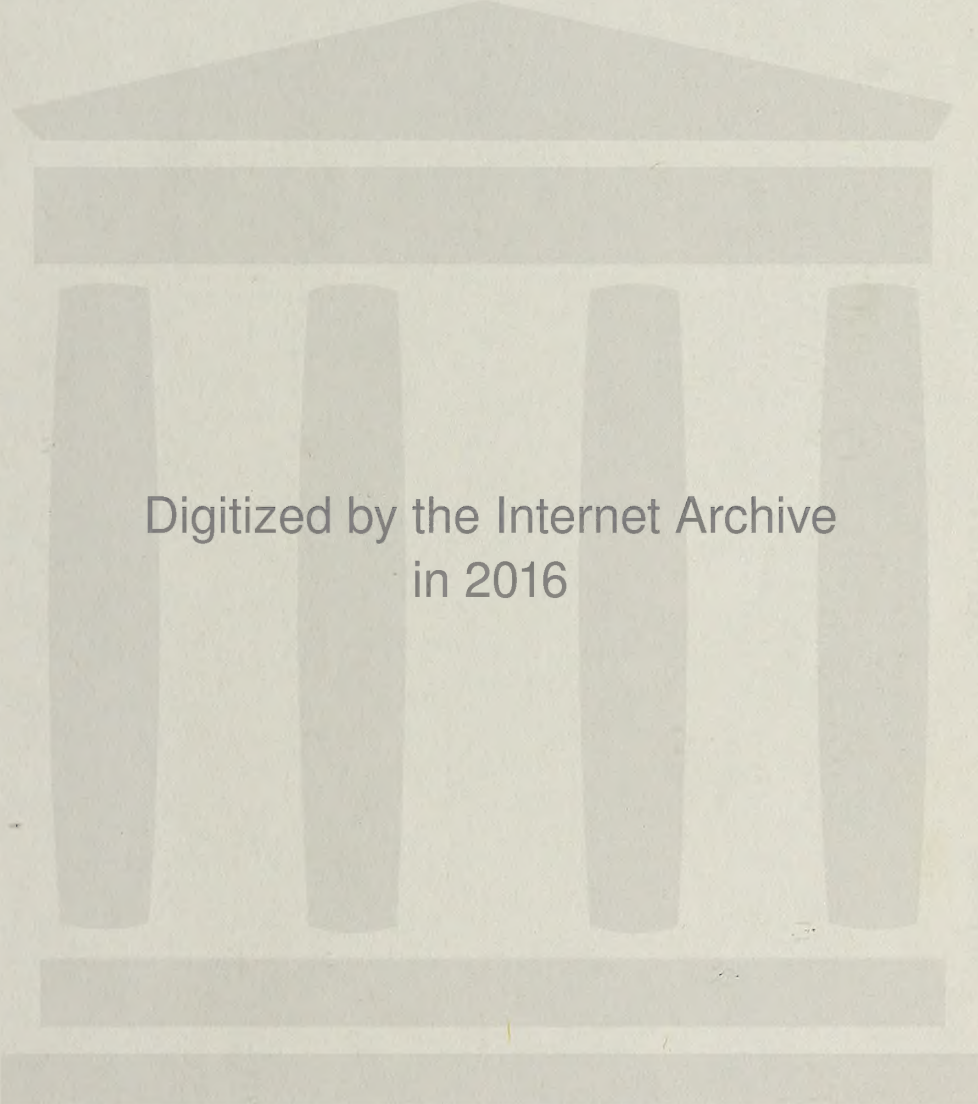


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# Connecticut Medicine

Connecticut State  
Medical Journal

Volume 30 / January, 1966 / Number 1



YALE-NEW HAVEN MEDICAL CENTER (see page 1)

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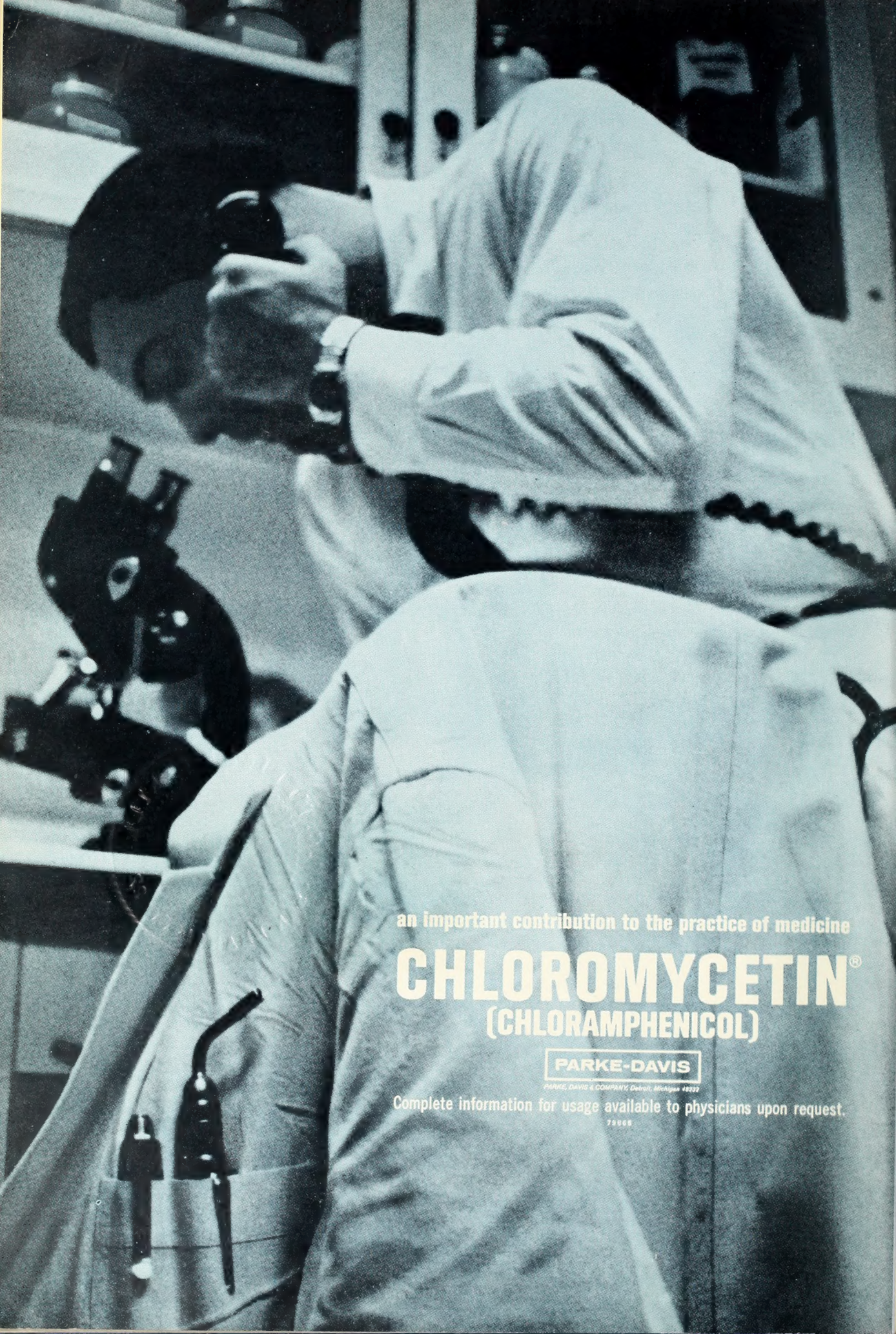
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# Connecticut Medicine

## editorials

### Renal Mechanisms For Both Raising And Lowering Arterial Pressure

We know that the kidney influences the level of arterial pressure, but we think of this in terms of kidney disease and its effect in producing hypertension. Narrowing of a renal artery experimentally will cause a rise in arterial pressure. This is now recognized as being caused by liberation of renin by the juxtaglomerular apparatus. In the blood renin comes in contact with the plasma globulin angiotensinogen and angiotensin I is split off. This decapeptide becomes converted in the plasma to angiotensin II an octapeptide with powerful pressor properties. By this mechanism the kidney is able to raise arterial pressure. Surgical correction of a narrowed renal artery often produces a complete cure of an existing hypertension. Does the normal kidney influence arterial pressure?

There is a large body of evidence that another mechanism in the kidney is able to lower arterial pressure. Goldblatt<sup>1</sup> recognized both a hypertensive and an antihypertensive action by the kidney for he observed that in artery stenosis to one kidney only transient hypertension resulted whereas when he removed the normal kidney severe sustained hypertension often evolved. It appeared to him as if the contralateral kidney had been exerting an antihypertensive effect.

A pure reduction in renal mass without renal artery stenosis also produces a rise in arterial pressure. Apparently one needs a certain renal mass to keep the pressure down. Furthermore, removal

of both kidneys leads to a rise in pressure developing quickly and not accounted for by mere salt and water retention. One needs the kidneys to keep the pressure down.

The best evidence for a hypotensive effect of a normal kidney is obtained from transplanation in humans. When one identical twin with severe hypertension resulting from chronic glomerulonephritis received a transplant of a normal kidney from the other twin, it brought about the disappearance of his hypertension.<sup>2</sup> Likewise, in the renal hypertensive rat, Gomez, Hoobler, and Blaquier<sup>3</sup> have shown that this same type of blood pressure reduction can be brought about with a normal kidney in the course of an hour.

Since the kidney appears to have mechanisms for both raising and lowering arterial pressures, can it be that they are geared to each other to provide thereby an integrated response for the control of arterial pressure? Such a concept is well established in biology. There are the integrated actions of the sympathetic and parasympathetic nervous systems, the alpha and beta cells in the islets of Langerhans and numerous others.

Tobian, et al, reasoned that if the level of arterial pressure is somehow registered in the kidney, then a high level of perfusion pressure should stimulate the antihypertensive action of the kidney and inhibit the release of renin. On the other hand, perfusing the kidney with a lower than normal pressure should inhibit the antihypertensive action and stimulate the release of renin. To test this hypothesis they used rats with renal hypertension. In

## THE COVER

### YALE-NEW HAVEN MEDICAL CENTER

A RECENT aerial view of the Yale-New Haven Medical Center showing the new Laboratories of Epidemiology and Public Health (upper right behind smoke stacks), the recently completed Charles A. Dana Clinic and Hospital Diagnostic and Service Building (lower center) located at main hospital entrance on Howard Avenue, and the Laboratory of Clinical Investigation under construction at the corner of Howard and Davenport Avenues.



eleven experiments an isolated normal kidney was perfused with the full force of the hypertensive blood pressure levels. After two hours there was a distinct drop in the arterial pressure of the hypertensive rat to a level one-third of the way toward normal.

In thirteen experiments an isolated implanted normal kidney was perfused at low normal pressures in the rat with renal hypertension. No drop in pressure in the hypertensive rat was observed. Apparently, the hypertensive mechanism of a normal kidney behaves appropriately, being brought into action by a high arterial pressure and being held in check by low normal pressures.

There thus appears to be a feedback arrangement in the kidney which is designed to maintain normal arterial pressure. How the antihypertensive mechanism acts is at present speculative. We certainly know more about the renin-angiotensin mechanism than about the renal anti-hypertensive mechanism. Does it act by the elaboration of a humoral substance which lowers blood pressure? Does it act by metabolic alteration or destruction of a circulating pressor agent? We await with great interest the answer, for it might open up a new field in acute hypertensive therapy.

L.H.N.

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## Science Tools:

### 13. Urinary Specific Gravity During Excretory Pyelography

It is well recognized that the urogram, particularly in early films, can give valuable information concerning the differential abilities of the two kidneys to excrete the contrast medium. However, often the estimation of the function is clouded by variables, such as the state of hydration, bowel preparation of the patient, the radiographic technique itself, particularly in the radio opaque substance employed, as well as the degree of calcification of the bones. As a result the radiologist, particularly in cases of poor opacification, might be

unable to differentiate between impaired renal function and the variables intrinsic to the study itself. As a result absence of opacification could reflect anything from slightly to markedly impaired function. Because of these inherent difficulties, the radiologist may find it necessary to repeat the procedure with an inevitable time lag for the result, and increased expense to the patient as well as additional vein punctures. All of which could be avoided if the interpretation of the radiographic findings could be combined with another objective measure of renal function carried out at the same time.

It has been noted since Bamrucker's study in 1942<sup>1</sup> that the specific gravity of the urine is considerably elevated for a prolonged period after intravenous injection of a contrast medium for excretory urography. This increase in the specific gravity is a measure of the concentration of the excreted contrast medium in the urine. Other methods for measuring the excreted radio opaque material on the urine have been related to its amount. If, however, the amount determines the increase in specific gravity, then this simple test would seem to offer valuable information. The changes in specific gravity of the urine before injection and sometime after then could supply a valuable adjunct to the information obtained from the excretory urogram. Marshall<sup>2</sup> has reported his study of 102 patients which has produced evidence that just determining the specific gravity of the urine before injection of the radio opaque dye and sometime after, is sufficient to reflect the renal function accurately.

All his patients had indwelling catheters and were given 30 cc. of 50 per cent of sodium diatrizoate intravenously and the urine was examined with a hydrometer for specific gravity at prescribed intervals for volume and specific gravity. He then compared the increase in the specific gravity of the urine over the preinjection level with other renal functional tests such as phenolred (PSP) and levels of serum creatinine. He found a highly significant correlation between the increase in specific gravity of the urine after the injection of the contrast dye and other tests of renal function.

Aside from routine preparation for the excretory urography, the patient merely voids before the test. The specific gravity of this specimen reflects the state of hydration of the patient at the time of the study. A second urine specimen is obtained just prior to the post-voiding film and its specific gravity is also determined. This allowed a measure of the increase that has occurred from the excreted contrast material in the urine. When he compared the degree of opacification of the pyelogram with the increase in the specific gravity of the urine, he





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found a very close correlation; the more intense the opacification of the urogram, the higher were the mean values of the increase in specific gravity. The data suggest that an increase in urinary specific gravity of 0.025 units or more would indicate a normal renal function. It is an excellent objective measure obtained with ease at the time of excretory urography.

In a community situation as distinct from a hospital situation with its easily accessible equipment for determination of renal function, it is not at all uncommon for the physician to send the patient to the radiologist for an excretory urogram without having performed any previous tests on renal function. If he should use the measure of increase of specific gravity in the urine in conjunction with the urogram, it would allow the radiologist to provide a quantitative measure of renal function along with the pyelographic findings and besides it would avoid necessity for repeat films and the time lag involved, not to mention the additional expense. Since the test is accurate and simply performed, requiring only a hydrometer and two specimen bottles, it is likely that it will become an essential part of all future intravenous pyelography.

L.H.N.

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## Assessment Of Drug Safety

In our generation of research and practice, modern therapeutics and the assessment of the safety of these remarkable new drugs have been greatly advanced. Dr. Beyer in a recent symposium on drug safety<sup>1</sup> points out that the safety of any drug can be assessed sensibly only in terms of what it is intended to do and that regardless of the drug, it will appear to affect some patients adversely. Even bed rest has been called a most dangerous of therapeutic procedures and without doubt so it is in many situations. He asks several questions such as: What happens after the "delight of discovery" of a new drug?; Is the preclinical safety valuation adequate?; When is a clinical trial indicated?; What safety factors must be considered?; How are long-term clinical trials conducted? We, in whose hands a new powerful drug is finally placed for clinical use, could greatly benefit by being aware of the answers to these questions.

Dr. Peck discusses what happens when a new compound is chosen for clinical trial. First, the pharmacologist undertakes to determine how useful it may be from his animal studies, and the toxicologist how toxic it is for animals. The next step involves a reconciliation of the efficacy and toxicity, to determine elements of safety and whether a new and interesting chemical may merit clinical trial. How safe the drug is for general use in therapeutics requires a third factor—judgment. Here one asks oneself "for what purpose is the drug intended?". Then we come to a clinical decision. From the results of the preclinical studies, the clinician is already alerted to the fact that certain side effects might be encountered in man; that which comes from overdosage; so-called secondary attributes; hypersensitivity reactions; and true toxicity. All of us who are in practice are well aware from our own experience the meaning of each of these untoward reactions.

Dr. Peck then goes on to give us a view of how preclinical investigation of the safety of a new drug is designed to define its toxicological attributes. They include single dose studies, short-term and long-term toxicity studies. In each instance, a physical examination, hematological, biochemical, organ function, and metabolic studies are performed. In the subacute and chronic toxicity studies extensive post-mortem studies are undertaken.

The acute toxicity studies are carried out in two or more animal species by different routes as single doses, large enough to be in the lethal range. The subacute and chronic toxicity studies are similarly conducted in one or more species. The general physical condition is closely observed. The organ function, including blood, the effect of the drug on metabolism, its speed of absorption, elimination and distribution and degradation are carefully determined. Of course, different animals may metabolize the drug differently. Then there is a search for the effect on enzyme systems, whether tolerance occurs, what does it do to the normal healthy constituents and whether the effects are reversible. Examples are given such as inhibition of cholesterol synthesis, which however may produce increased amounts of toxic precursor desmosterol with abnormal deposits of this steroid; inhibition of monoamine oxidase systems with resulting damage to the liver and suppression of corticotrophin secretion by some steroids. Pathological studies are carried out to reveal anatomic alterations. This helps the search for a dosage level at which such changes are not produced.

To study the effects on reproduction require three basic experimental designs. Single generation study in established pregnancy in which the drug is



administered at a preselected time. Multiple generation experiments is a second design in which each new generation of animals is bred to produce new litters. The drug is fed before breeding and throughout the reproductive cycle. In this way are observed drug effect on fertility, implantation of the ovum, development of the embryo and fetus, abortion, delivery, number of live births and the size of the litters. Thus we get a view of teratogenesis, viability of the newborn, growth of the young, and quality of the mother's milk. The evaluation of these results permits estimation of the risk involved in the administration of a new agent to man for the first time.

Dr. Kohlstaedt makes clear that the initial clinical trial must be a well controlled study and should be conducted by a physician who is trained in this form of clinical research and should be performed in an environment that permits accurate observation, since it involves a reproduction of the testing on man that had previously been performed on animals. Man's reaction to the drug might be different and certainly the doses employed would have to be smaller. Because of the similarity in clinical and preclinical trial, there is required a close liaison between the physician who will evaluate a drug and the scientists who participated in its preparation and testing in animals.

The number of compounds being synthesized by chemists and being isolated from plants and the soil is augmenting the need for clinical trial, while the number of competent investigators with adequate research facilities lags behind. As a result, research units are badly needed to provide the proper environment and personnel competent to conduct initial clinical trials. There must be hospital wards with specially created laboratories for chemical and bacteriologic tests. Dr. Kohlstaedt insists that only a full-time physician can plan and conduct the studies and himself observe the patients adequately during the clinical trial.

He then proceeds to lay down certain ground rules for clinical trial. First, that it is never safe to extrapolate the dose from animal to man, but that drugs must be given separately starting with a small dose and gradually increasing it. Second, that sometimes it is desirable to test the drug on normal humans except, in trial of a drug for malignant disease, when very little can be accomplished in a normal person. Third, he emphasizes the need for eliminating bias in the early stages of evaluation (appraising the appraiser<sup>2</sup>). Fourth, if the drug is found to be active, the next step is to increase the amount to establish a "dose response." Finally, the drug should be compared with a known drug and again with a placebo (placebo-phenomenon<sup>3</sup>) in which double blind techniques are used. After the

initial clinical trial is complete, it is customary to discontinue it in man and go back to give large amounts to more than one species of animal. When sufficient evidence of its safety has been accumulated, the second phase of the trial is undertaken at which time it is placed with several competent investigators for adequate trial periods.

Dr. Friend recapitulates what has already been stated and discusses moral, legal, and administrative aspects. The utmost care should be taken to protect experimental animals from pain, suffering, or any form of inhumane activity. Second, that no agent should be given to a human subject without his consent or those responsible for him. The trouble here is that this is possible only when enough is known about a drug to be reasonably certain of its action. We all know that it is impossible to be certain how a drug may act on a man from the way it acts on animals. Therefore, it is often not possible to secure truly "informed consent." Dr. Friend thinks the most satisfactory method is to have a very frank discussion with the subject, explaining what is being done, what we know about it, why the agent is being studied and probable action, and any known risks. Just having the patient "sign a consent paper," however, will probably not spare a physician in a court of law.

Every wise physician knows it is the type of relationship he has with his patient that determines the attitude the patient will take, should some untoward effect occur. The conscientious, understanding physician employing his skill to the best of his ability, seldom encounters legal problems in practice. However, no drug suspected or known to make a patient worse should be given unless all parties fully understand the situation. No married female should be given an experimental drug unless repeated pregnancy tests show she is not pregnant or she and all concerned are willing to accept possible harm to the fetus. When all is said and done, Dr. Friend points out that there is far less risk involved in being a subject for a new drug study conducted by skilled investigators than in riding in an aircraft or driving an automobile.

Dr. Fries points out that a new therapeutic agent is good or bad in comparison to presently available therapy. His formula of merit of new drug is:

$$\text{Effectiveness} + \text{ease of administration} - \text{toxicity} - \text{tolerance} = \text{Merit}$$

He urges careful records, prompt report of toxicity to the sponsor of the new drug. This is the responsibility of the entire medical profession and should continue. It will help each of us to observe our cases carefully and intelligently. He does not believe that withdrawal of an effective drug should be undertaken prematurely if it is successful in the treatment of serious disease.





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## Precautions

Obtain a detailed history and a complete physical and laboratory examination, includ-

ing a blood count. The patient should be closely supervised and should be warned to report immediately fever, sore throat, or mouth lesions (symptoms of blood dyscrasia); sudden weight gain (water retention); skin reactions; black or tarry stools. Make regular blood counts. Use greater care in the elderly.

## Warning

If coumarin-type anticoagulants are given simultaneously, watch for excessive increase in prothrombin time. Pyrazole compounds may potentiate the pharmacologic action of sulfonylurea, sulfonamide-type agents and insulin. Carefully observe patients receiving such therapy.

## Adverse Reactions

The most common are nausea, edema and drug rash. Hemodilution may cause moderate fall in red cell count. The drug may reactivate a latent peptic ulcer. Infrequently, agranulocytosis, generalized allergic reaction, stomatitis, salivary gland enlargement, vertigo and languor may occur. Leukemia and leukemoid reactions have been reported but cannot definitely be attributed to the drug. Thrombocytopenic purpura and aplastic anemia may occur. Confusional states, agitation, headache, blurred vision, optic neuritis and transient hearing loss

have been reported, as have hepatitis, jaundice, and several cases of anuria and hematuria. With long-term use, reversible thyroid hyperplasia may occur infrequently.

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This overall view of how drug safety is evaluated helps to illuminate the field of drug therapy and how far we have gone in the protection of our patients from untoward effects of new and powerful drugs.

L.H.N.

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## Science Tools: 14. Carbon 14 Breath Excretion Studies

When radioactive material interacts with gas, electrons and positively charged nuclei are produced. If this reaction is produced in a closed metal chamber, the electrons may be collected on a positively charged probe producing an electrical current that can be measured and related to the amount of radiation passing through the chamber. If after ingestion of a Carbon 14 labelled metabolite, the subject's breath is continuously monitored for radioactivity, the amount of Carbon 14 O<sub>2</sub> recovered can then be correlated with the amount of the isotope administered and an estimation of absorption from the gastro-intestinal tract and utilization by the organism can be obtained.

Cozzetti<sup>1</sup> has studied breath excretion curves after the ingestion of Carbon 14 labelled actanoic acid in sixteen normal subjects and four patients with malabsorption due to cystic fibrosis. In the normals the average breath excretion in one hour was 12.6 per cent while in the malabsorptions breath excretion was only 5.1 per cent. This was repeated and in one normal it was 13 per cent in fifty minutes while it was 3.9 per cent in a malabsorption case in fifty minutes of breath excretion. Since the gastro-intestinal tract is relatively inaccessible and many difficulties occur with intubation when employed to study absorption, the method of breath excretion of radiocarbon is obviously an important quantitative measurement of the absorption and catabolic fate of foodstuffs that are labelled with radiocarbon.

Breath excretion curves were also obtained after the ingestion of Carbon 14 labelled carbohydrate. In two normal subjects breath excretion curves rose at a slow rate and reached a peak in 100 minutes. In an obese girl of fourteen, however,

excretion rose rapidly and remained elevated over a five hour study period. This obviously suggests an alteration of glucose utilization in obesity and in fact it was found that this child's glucose tolerance test was abnormal.

Lactase ingestion studies were also carried out. In a child with juvenile lactase insufficiency, breath excretion curves of C 14 O<sub>2</sub> flattened, indicating poor absorption and metabolism of the lactose. Cozzetti also studied the effect of giving either glucose or lactose on fatty acid absorption. In four normal infants, a prompt rise and sustained breath excretion of C 14 O<sub>2</sub> was noted over a sixty minute period when actanoic acid was given alone. However, when glucose was given with the labelled fatty acid then a delayed C 14 O<sub>2</sub> appearance was noted and cumulative breath excretion of C 14 was reduced. Similarly, lactose given with the labelled fatty acid also produced a reduction in appearance and cumulative excretions. The presence of glucose and to a lesser extent lactose, appeared to decrease the absorption of the fatty acid. Of course, alteration of the absorption may have been caused by preferential utilization of carbohydrate or delay in gastric emptying or perhaps factors that require further clarification.

It is clear that excretions of labelled C 14 O<sub>2</sub> from specifically labelled metabolites may be used to study certain metabolic functions in individuals of all ages. All one needs to do is to administer Carbon 14 labelled fatty acids, glucose, or lactose and monitor the excretion of C 14 O<sub>2</sub> over a limited period. This provides an estimation of the absorption and utilization of the substrate under study. Cozzetti points out that short chain fatty acids are absorbed and carried to the liver, whereas the sixteen or more carbon chains enter the lymph first and are then transported to the liver via the thoracic duct and the systemic circulation. In the high carbon chain fatty acids, then the lymphatic system must also be free to produce normal breath excretion studies.

The half life of carbon 14 is exceedingly long but the significant biological half life of radio carbon is quite short, from six to twenty-four hours. The dose range of 1 UC to 2 UC employed in these studies is very small and in general, the excretion began to decrease at the end of two hours and at the end of six hours, radiocarbon could no longer be detected in the breath. The radioactivity in samples of blood and urine from these subjects was too low to be detected in a liquid scintillation counter or with a strip counter. It is only after C 14 O<sub>2</sub> accumulated in the breath over a period of time that its detection became possible.

Breath excretion studies of C 14 is therefore an effective method in investigating the catabolic fate



of carbon in the living organism as the results of Cozzetti's studies clearly show.

L.H.N.

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## Pathogenesis Of Myocardial Necrosis

There is a good prospect that in the not distant future we will come into possession of a drug that can lyse thrombi. It is therefore time to consider several problems in connection with the utilization of such therapy. One is, in what patients such therapy could be expected to yield beneficial results. Another is whether once thrombosis has taken place, especially in arterial disease, whether any benefit can be expected from such therapy, since infarction has already occurred. A third problem is how long thrombolytic therapy should be continued since thrombosis may be expected to reoccur in a vessel whose endothelial lining has been injured at the location of the previous thrombus. Finally, especially in coronary artery disease, infarction at times assumes a controversial aspect in situations which give rise to liability claims.

One common aspect of all these problems is whether thrombosis has actually taken place in a given case of myocardial necrosis, not after the necrosis but before. Such an answer would be available if we had a reliable test for thrombosis at an inapparent site, a test not now available. The diagnosis of infarction is in itself not too difficult, but all it tells us is that a vessel is closed or almost closed, not whether the closure is the result of an occluding thrombus. It is universally acknowledged that occlusive disease of the coronary arteries almost invariably accompanies infarction of the myocardium. But we are unable to tell during life the frequency of thrombosis in such a case. This difficulty understandably exists in a living patient, but it is also reflected even in the reports of competent pathologists, in which the incidence of thrombosis ranges from 21-85 per cent! Some of these variations must be attributed to technical difficulties in dissection, post-mortem artefacts and absence of agreed criteria for the definition of arterial thrombosis. Nevertheless, a resolution of the variable and contradictory results of these investigations is a necessary precondition for the establishment of a strong base for future research into the pathogenesis and therapy of this important disease.

In an attempt to resolve these difficulties, Ehrlich and Shinohara<sup>1</sup> describe the results of microscopic

examination of serial blocks of previously unopened, fixed, and decalcified specimens of the entire extra-mural coronary arterial tree. They observed rigid criteria in the microscopic differentiation of thrombi from clots. These authors analyzed sixty-seven hearts, twenty-nine without infarcts (controls) and thirty-eight with acute infarcts. They found unequivocal thrombi in half of the thirty-eight acutely infarcted hearts, but in only ten of these did the thrombus occlude the lumen which was not already narrowed down to less than one-quarter the original calibre. Previously Branwood and Montgomery<sup>2</sup> had sectioned sixty-one infarcted hearts from apex to base at 2 mm. intervals and found occlusive arterial thrombi in thirteen hearts and mural non-occlusive thrombi in an additional twenty-three. These authors concluded that "the thrombi found at post-mortem in coronary arteries, is sometimes not the cause but the terminal event in an established infarct."

It is significant that in half of the cases no recent thrombi were found and in only one-quarter were the thrombi totally occluding a lumen of significant calibre. This makes it necessary to reassess traditional concepts of the significance of recent thrombi in the coronary arteries of hearts with recent infarcts. We employ the term infarct to a more or less circumscribed area of tissue necrosis. Clearly the lesion can result from any form of regional vascular insufficiency as well as thrombosis. This must inevitably direct our attention along the lines of more recently elucidated factors such as neurovegetative and rheologic disturbances and other as yet obscure mechanisms.<sup>3-7</sup>

It is clear that in at least half of cases a thrombus is not the precipitating cause of infarction and thrombolytic therapy would be ineffective. Obviously until we come into possession of a test for thrombosis at an inapparent site, thrombolytic therapy if given to all in cases of acute infarction can at best benefit only half of the patients. This makes it more urgent that a thrombolytic drug should not have any significant side effects. Since such therapy can at best affect only half of the patients favorably, statistical studies on the value of such therapy should recognize this inherent difficulty in any such investigation.

If one undertakes thrombolytic therapy, it is obvious that after clot dissolution one would require a period of anticoagulation therapy to prevent rethrombosis at the original site of thrombus formation since the endothelium is generally impaired at the thrombus site and epithelialization takes time. If a thrombus was present and its lysis reestablished the continuity of the lumen, then one would expect definite benefit since nutrition of





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the peri-infarction zone would improve and diversion of blood from other areas of the heart would not become necessary to support a collateral circulation.<sup>8</sup> This latter point is especially significant since from Ehrlich's studies we learn that in addition to the main area of infarct, focal muscular necrosis was extremely widespread. In only nine hearts was necrosis confined to one chamber while in the remaining twenty-nine hearts 2-3-4 chambers were involved. In such instances blood diversion from an already compromised area to an infarcted one could prove disastrous.

Clearly we are entering a period in our knowledge about myocardial infarction which require further investigations into the pathogenesis of myocardial necrosis. Can there possibly be factors which we have not credited with much influence in the production of this serious illness, such as autoimmune disease, neurovegetative disturbances and perhaps others as yet obscure?

L.H.N.

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## Circulatory Difficulties Caused By Atrial Fibrillation

Atrial fibrillation is the commonest arrhythmia associated with heart failure. In general, with digitalis, diet, rest and diuretics the heart failure can be readily corrected. Nevertheless, the atrial fibrillation tends to remain. It is therefore important for the physician to recognize the hemodynamic abnormalities imposed on the circulation by this arrhythmia alone.<sup>1</sup> Can it be of sufficient magnitude to support the contention that, in and of itself atrial fibrillation is a real disadvantage to the circulation. With the advent of a new method for converting arrhythmias to regular sinus rhythm, namely external cardiac electrical shock,<sup>2, 3</sup> it is

now imperative that we examine the value of restoration of atrial function in cases of atrial fibrillation in whom the atria are dilated, and non-functional. In atrial fibrillation the blood flows from the atrial into the ventricles during diastole. Without atrial systole there is poor emptying of this chamber. There is a tendency for sludging of blood in relatively passive pools and this favors the formation of clots which is known to be a common complication of this rhythm. If there is also superimposed tricuspid or mitral insufficiency in atrial fibrillation, not all blood in the ventricles will move forward during systole; there will be blood moved into the atria producing turbulence, stasis and contribute further to the formation of clots. Besides, the cardiac output is decreased following onset of atrial fibrillation and this may compromise blood flow to such vital areas as the brain, kidneys and heart itself. The symptoms arising from this disturbance are well known especially such as general body fatigue and those arising from the nervous system, giddiness, change of memory. Then there are less symptomatic but equally fundamental dysfunctions such as retention of Na and K as well as altered liver function.

These circulatory difficulties caused by atrial fibrillation are compounded by the absence of the mechanical shortening of the atrial fibers, since it is well established that atrial systole is needed to preserve the competence of closure of the A.V. valves.<sup>4-9</sup> In short, atrial systole not only helps in the proper closure of the A.V. valves but it also contributes a physiologically important volume to the nearly full ventricle thereby increasing the ventricular tone before contraction. In those two respects atrial systole acts as a vital regulator of stroke volume.

If this is true then conversion of atrial fibrillation to regular sinus rhythm in patients who are in congestive failure should add an important element to the reserve of the ventricle. We might expect that in some patients with an irreversible stage of heart failure, restoration to normal sinus rhythm may actually be a turning point leading to improved exercise response and this in fact has been emphasized by Ferrer and Harvey,<sup>1, 2</sup> by Freeman and associates<sup>10</sup> and many others.

There are of course certain patients in whom conversion may be difficult or impossible or in whom regular sinus rhythm once achieved will not persist. This is most likely to occur in patients whose atria are greatly enlarged or those in whom the myocardium is damaged by extensive inflammation, post-operative pericarditis, or by sutures after operation as well as widespread chronic fibrosis. If we recognize this fact the question presents itself as to how much weight we should attach to these



difficulties in making a decision for or against correction of atrial fibrillation.

During the early post-operative period after pulmonary pericardial or cardiac surgery the prophylactic use of quinidine in all patients who are likely to develop atrial fibrillation has been highly successful in preventing this arrhythmia.<sup>1</sup> Ferrer and Harvey start quinidine at about the sixth or eighth post operative hour unless the blood pressure is low or falling. Until the patient is eating well, the intramuscular preparation is used and then the oral drug is substituted. Although there are recognized disagreeable effects from this drug in some patients, the untoward effects can be monitored by the electrocardiograph with great precision. Once atrial fibrillation has occurred the newer electric shock therapy by D.C. defibrillation can cause reversion to regular sinus rhythm with at most only modest side effects under light anesthesia. In some instances it has even been possible to defibrillate without general anesthesia and with very little discomfort to the recipient.<sup>3</sup>

The danger most feared in relation to conversion of atrial fibrillation is of course the loosening of emboli into the circulation. The present explanation of this phenomenon is that particles adherent to the endocardium are dislodged by the mechanical jarring consequent to resumption of atrial systole during which there is increased velocity of flow. The late embolic accidents occurring many hours or days after conversion are those in which atrial systole requires some time to work the particles loose or dislodge them from a pedicle. We must not forget the possibility that atrial fibrillation has returned and again subsided without being detected.

There remains a need to obtain further data on a hemodynamic explanation for the embolic complications. Perhaps long electrocardiographic monitoring devices which operate twenty-four hours a day may help to solve the problem. Likewise, hemodynamic studies on patients immediately before and after electrical conversion are needed to further clarify what happens in early or late embolization. Certainly from what we know of the function of atrial systole, maintenance or reversion to the normal rhythm is warranted in a larger percentage of patients. For this reason the difficult aspects involved in therapy to maintain regular sinus rhythm deserves continued study.

L.H.N.

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## The Control Of Cancer By Endocrine Methods

Huggins<sup>1</sup> in an address delivered when he received the Passand Award summarizes his brilliant and extensive experiences with hormonal treatment of advanced cancers. In the therapeutic destruction of certain cancer cells in the living host, two principles have been evolved: one hormone interference, and another, hormone deprivation with a steroid mechanism essential for the life of the cell.

It had already been known since Beatson's report of 1896<sup>2</sup> that advanced cancer of the mamma can be induced to regress after oophorectomy and he advised to "look in the female to the ovaries as the seat of the existing cause of breast cancer." But though this observation was prescient the explanation of the phenomenon was not simple. Breast cancer also thrives in the male and benefits of great magnitude frequently follow orchiectomy in the human male.<sup>3</sup> Clearly testicular function can also sustain mammary cancer. So can an adrenal factor since bilateral adrenalectomy can result in profound and prolonged regression of breast cancer in men and women who do not possess gonadal function.<sup>1</sup> A final confusion arose when Haddow, et al.<sup>5</sup> found that phenolic estrogens can have an ameliorative effect in human mammary cancer.

This paradox that hormones can be both activating and suppressive of breast cancer was not easy to resolve. In the rat as a test animal large amounts of ovarian hormones in combination completely destroy many of rat's mammary cancers





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while at the same time its normal mammary glands proliferate. The cancers were induced by irradiation and finally by a simple feeding of a special hydrocarbon 7, 12-DMBA. The cancers ensue rapidly and invariably and their numbers are very large. Here then was an excellent test model for studying hormone dependence. Then it became clear that the cancers accelerate in pregnancy and following administration of progestational compounds. However, if estradiol is administered also in large doses it delays the appearance of the cancer. When this combination of estrogen and progesterone was given to a rat with induced cancer, many of the mammary cancers were completely eliminated and over half were still free of the tumor six months after steroids had been discontinued.

This experimental lead led Landou, et al. to treat 15 patients including one man with disseminated breast cancer. With a daily intramuscular injection of 50 mg. progesterone and 5 mg. of estradiol benzoate he induced a measurable and clinically worthwhile improvement in nine of 15 patients who had already undergone other forms of endocrine therapy such as adrenalectomy and oophorectomy. The question of course arises why were the others not responsive to hormone therapy.

The sad fact is that mammary cancers induced in the rat become independent later in their development. Furthermore, in a different species—the mouse—the mammary cancers are rarely hormone dependent. Perhaps in man some people have hormone dependent breast cancer and others hormone independent tumors, especially in the late stages of their development. Obviously the remaining great problem in mammary cancer is understanding and controlling hormone independence of malignant cells. The paradox mentioned above about breast cancer thus arises from the fact that the tumor is hormone dependent only in the early stage and excessive amounts of two hormones, not one, seem necessary in this phase to control the growth.<sup>6</sup>

Another example of the value of excessive amounts of hormones to destroy cancer cells comes from the experience with the use of cortisone and related steroids in the treatment of lymphoma and leukemia. This goes back to the classic work of Dougherty and White<sup>7</sup> on the lytic action of ACTH on lymphoid cells. When this technique was applied by Hedman and Kendall to mice bearing a transplanted lymphosarcoma, they observed dramatic and apparently complete cures which, however, were only temporary in a majority of animals. The same temporary repression in certain cases of human leukemia and Hodgkins disease was observed by Pearson, et al. after administering

ACTH. Thus we see that cortisone induced regression of lymphomas does not differ in principle from the effect of corticosteroids on the lymphocytes of normal animals.

The second principle hormone deprivation is classically illustrated by the effect of testosterone in supporting prostatic cancer and the regression that takes place in this tumor by testosterone removal or estrogen excess. The good fortune of Huggins and his group was the discovery that the dog is the only laboratory animals in which tumors of the prostate occurs. As in man, it is very common to find spontaneous tumors in the prostate of the aged dog. In animals with an interstitial cell tumor of the testis a prostatic neoplasm is certain to be found. They soon found that orchiectomy or administration of restricted amounts of phenolic estrogens caused a rapid shrinkage of canine prostatic tumors. These findings proved applicable to patients with prostatic carcinoma.

What led the investigators to recognize the crucial role of testosterone in prostatic function was the observation that following orchiectomy the prostate shrinks, the oxidative phase of carbohydrate metabolism declines and secretion stops. Testosterone corrects these defects. The cycle of growth and atrophy induced by providing or withholding testosterone was repeated many times in the course of the life of the castrate dog. The prostatic cell does not die in the absence of testosterone. It merely shrivels. The hormone dependent cancer cell is entirely different. It cannot participate in growth cycles since it dies in the absence of supporting hormones.

What helped in the study was a test for acid and alkaline phosphate in the blood. Kutscher and Wolbergs<sup>8</sup> found that the prostate gland is rich in acid phosphatases. As long as the tumor is limited to the prostate the acid phosphatases do not rise. Once the tumor has metastasized then significant increase of acid phosphatases is found in the blood. Furthermore, if the bone is invaded then alkaline phosphatase liberated in bone destruction also rises. Here then we have a test model to determine regression in metastases that may follow therapy. A simple model that offers objective evidence of regression or progression of the disease was of inestimable help for the Huggins group to follow the effects of hormone deprivation upon the course of prostatic cancer.

It thus seems clear that the control of cancer by endocrine methods derives from the recognition that hormones or synthetic substances that induce similar physiologic effects are of crucial significance for the survival of several hormone responsive cancers of man and animals. Opposite sorts of change of the hormonal status can induce regression and in



some instances cure of such cancers. These modifications are deprivation of essential hormones and hormone interference by large amounts of critical compounds.

L.H.N.

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## Tetracycline A Teratogen?

The undesirable effects upon the neonate of sedatives administered to the mother during labor is now well documented.<sup>1</sup> This information has lent impetus to a movement utilizing "natural" childbirth and even hypnosis by some obstetricians during labor. Since the thalidomide tragedy we have all worried about what effects other ordinarily harmless drugs may have upon the fetus.

There are difficulties and limitations that are encountered in testing the teratogenic effects of drugs on the fetus and this has prompted many attempts to study teratogenesis with tissue cultures. Many physiological compounds and certain toxic agents have been studied this way including two compounds that interfere with osteogenesis. Tests with both thalidomide and lathyrogenic compounds in organotypic cultures show effects that resemble those known from in vivo experiments.

The studies on the teratogenic effects of tetracycline reported by Saxén<sup>2</sup> were undertaken for several reasons. In the first place it was already known that this antibiotic is transmitted from the maternal to the fetal organism where it is incorporated by the skeleton especially in the zones of active bone formation. In the second place its retarding effect on the growth of embryonic bones has been

observed in experiments with animals and in premature infants. This suggested that the drug is a true teratogen. Accordingly Saxén undertook to examine these effects under controllable conditions in vitro.

Ulnar and radial bones of 14-16 day old mouse embryos were dissected aseptically and cultivated in a special medium. He then added tetracycline in various concentrations, keeping the pH optimum. The bone rudiments, both controls and those treated with various concentrations of tetracycline, were harvested after cultivation for 3-12 days and then analyzed by special techniques.

The effect of continuous treatment with tetracycline in concentrations of .01 to 100 micrograms (ug) per ml was to prevent increase in the length of the mineralized zone, and also produced a shortening of the calcified zone and a decrease in the calcium content of the previously mineralized zone. The effect was reversible if the treatment were of short duration but not after prolonged presence of tetracycline. Saxén found further that in all experiments in which tetracycline treatment was interrupted after 3-4 days subsequent development resulted in severe malformation.

Histological studies were carefully carried out with appropriate techniques. The findings varied greatly and clearly correlated with the stage of osteogenesis at the time of explantation and onset of tetracycline treatment. If the rudiments had already become mineralized, then by special techniques, tetracycline was found in the calcified zone. If mineralization was not apparent at the time of explantation and in which tetracycline completely prevented onset of mineralization, then no calcium was detected when proper techniques were used for its recognition.

It is clear that in organotypic cultures, tetracycline in concentrations comparable with those attained by therapeutic doses, (1 ug per ml was sufficient to produce the effect), has an inhibitory effect on the mineralization of embryonic bones as well as producing maldeveloped bones. The mechanism of this interference is not yet clear. It can't be just that tetracycline forms a complex with calcium ions since no calcium at all is deposited when treatment is begun before the onset of calcification. Saxén, however, found no diminution in soluble or ionic calcium in the medium during 12 days of cultivation in the presence of tetracycline. The conclusion seems valid that tetracycline prevents the incorporation of calcium by embryonic bone.

Clearly cultures of rudiments of embryonic bone seem to afford a valuable tool for the exploration and analysis of certain toxic and teratogenic effects of drugs. At this stage it should be stressed that the



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#### References:

Teichmann, W. O. and Horvath, P. N.: Southern Medical Journal 50, 1521 (1957).

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conclusions reached from such studies are not yet applicable on the clinical level. However, knowing that tetracycline can pass from the maternal to the fetal circulation, that in vitro it can produce teratogenic effects on bones in the same concentrations that are achieved with its use clinically what brave soul would be willing to give tetracycline to a pregnant woman until all doubts are dispelled?

L.H.N.

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## Science Tools: 19. Radioisotopes In Cardiology

Skilled cardiologists rely on a history of the patient's illness and careful physical examination including chest X-rays to form a rough approximation of several measurements of cardiovascular dynamics such as velocity of blood flow, cardiac output, intracardiac blood volumes, pulmonary blood volumes and reduction in the coronary circulation. The question then arises as to whether there are any isotopes techniques available at the present time that are really useful in the care of patients. There probably are, but the practical application has lagged because for a while the crude nature of counters and radioactive tracers and also the requirement of a special federal license to use isotopes.

Historically the use of isotopes in cardiology antedates the artificially prepared ones made in the cyclotron and furnished to investigators by the Atomic Energy Commission since World War II. For example, Blumgart in 1927<sup>1</sup> used radium C and a cloud chamber to determine the velocity of blood flow. When man-made isotopes became available it became possible to measure rate of blood flow through tissues. In 1949 Prinzmetal, et al.<sup>2</sup> placed a geiger counter over the precordium to follow the circulation of a bolus of radioactive albumin combined with  $I^{131}$  through the right and left sides of the heart. This he dubbed Radiocardiogram. Then in 1953 Waser and Hunzinger<sup>3</sup> made the first attempt to measure coronary blood flow by labelling coronary blood with isotopes. Since then several successfully developed methods, not yet used by clinicians, have been used experimentally. From radiocardiogram it is possible to determine cardiac output, the amount of blood in the lungs, the relative amounts of blood in the right and left side of the heart. All that is needed

is a single injection of  $I^{131}$  albumin and inexpensive counting equipment.

The heart scan is at present the most useful isotope technique.<sup>4</sup> The circulating blood can be effectively labelled by a single injection of  $I^{131}$  albumin and the intracardiac pool outlined with the use of a commercial scanning apparatus designed for thyroid studies. The usual clinical question is to determine whether a large heart shadow is caused by dilatation of the heart or by pericardial effusion. If only dilatation of the heart is present, the entire area corresponding to the heart shadow appears radioactive. If pericardial effusion is present, the blood pool is normal in size even though the heart shadow is enlarged. The technique is also sensitive to the presence of myocardial hypertrophy although the clinician does not need this kind of test to form an accurate judgment of hypertrophy which he can obtain from physical examination, electrocardiographic changes and chest X-ray. Finally, it should be mentioned that a more accurate outline of the blood pool could be useful in detecting aneurysms of the left ventricle, pericardial cysts and loculated pericardial effusions.

The amount of blood in the lungs can be determined by radioactive blood, but here again the clinician has good ways of estimating increase in this measurement by simpler means of detecting cyanosis, measuring a reduced vital capacity, dyspnoea, reduced motion of the diaphragms and rales at the bases. Similarly an obstruction of a certain segment of a lung either by a pulmonary embolus or pneumonitis or lung cysts can be detected by injection of precipitated radioalbumin. A non-radioactive zone corresponding to the unperfused lung will show up in the scan. Here again the result would not be too helpful to the clinician since he has equally good methods of making the differential diagnosis. It may perhaps be used in cases of suspected embolization in which no change is made out in the routine radiogram.

It is of extreme importance to be able to measure the rate of coronary blood flow in man especially now that single segmental stenosis of a coronary artery is capable of surgical repair. There are presently three methods of estimating coronary blood flow by isotope techniques. One is by measuring how fast an isotope, when injected into the blood, is taken up by the myocardium. Another method is to follow a bolus of tagged blood as it flows through the coronary vessels. A third method is to measure the rate at which a freely diffusible inert gas is washed out of the heart muscle by the blood.

Single injections of  $K^{42}$  or  $Rb^{86}$  are taken up by muscle cells and although the method is sound

there is need for much improvement before clinical use. Measuring the coronary blood flow by identifying the isotope in the descending limb of the left ventricular portion of the radiocardiogram, is also for the future. Catheterization of coronary artery and coronary sinus and injection of a radioisotope is too ambitious a maneuver clinically. In fact, none of the methods measuring coronary flow have as yet been shown to be useful in the case of patients. To find a clinical role, a technique should make an earlier diagnosis of coronary artery disease or perhaps outline the extent of the obstruction to blood flow in the different arteries or make it possible to follow the effect of therapy on coronary blood flow. One real difficulty of course is that coronary blood flow is not greatly reduced in most people with coronary artery disease when they are at rest.<sup>5</sup> For this reason, to detect coronary narrowing by measuring blood flow it will be necessary to measure the response of the vascular bed to stress such as exercise. The clinician will not need heart scanning for such a purpose; he already has the patient's characteristic pain and anoxic changes in the electrocardiogram as excellent guide posts.

As for the future, we may expect as Love<sup>4</sup> points out much improvement in instrumentation, isotopes used, and reduction in their amounts needed, as for example, increasing the size of the NaI scintillation crystals so that they can pick up hundreds of times as many counts. There will be improvements in scintillation camera and autofluoroscope. Perhaps actual pictures of the distribution of the isotopes within the body will become possible. The present philosophy is to use quantity of tracers that deliver an insignificant dose of radiation by using isotopes that decay rapidly or are excreted rapidly.<sup>6</sup>

We know that scans of the cardiac blood pool are of practical value and will be widely used. Simple methods of measuring cardiac output and blood volume are available and are being used for investigation purposes but have not been exploited by clinicians for very good reasons. There will be rapid advances in nuclear technology and out of these may come practical and innocuous methods for measuring regional blood flow in the heart and other organs. Such methods will undoubtedly be used by clinical investigators to enrich our theoretical and practical understanding of what is going on in cardiovascular dynamics. As such we will watch developments in this rapidly expanding field with great interest. But whether the methods will lend themselves to direct clinical application will depend upon whether or not they provide a practical way of solving recognized medical problem.

L.H.N.

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## Laser Energy: Its Tumoricidal Effect

Laser is an acronym for Light Amplification by the Stimulated Emission of Radiation. The theory of amplification by controlled release of stored energy was developed by Townes and Schawlow in 1958. The first operational laser was built by Maiman in 1960 utilizing a synthetic ruby crystal. Extremely powerful energy densities and other unusual special properties are afforded by the intensely coherent, almost completely non-divergent beams of light.

The laser is vastly different from X-ray or gamma irradiation: principally laser energy is non-ionizing and also the laser can produce tremendously high flux densities.

To date a large part of the work that has been done has been experimental because of the obligation of the medical scientist to understand as completely as possible the biologic effects of this new form of therapy before clinical application. There is also an obligation to learn what effects laser energy may have on the operator so that we will avoid the disastrous consequences of the early use of the X-ray on the operator as well as on the patient.

In Deterling's laboratory,<sup>1</sup> the effects of ruby laser energy were studied on tumors implanted in the cheek pouch or flank of the syrian hamsters. Eleven tumors were of human origin, three of induced origin and six of autogenous hamster origin. The tumors were subjected to laser energy ranging from 50-1500 joules. Of the total, seven were cured, three half cured, three hardly affected and six showed negative results.

Careful studies on cell growth in tissue culture of conjunctival cells by Rounds and Chamberlain<sup>2</sup>





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possibly be increased by meprobamate. Grand mal seizures may be precipitated in persons suffering from both grand and petit mal. Prescribe cautiously and in small quantities to patients with suicidal tendencies.

**Side effects:** Drowsiness may occur and, rarely, ataxia, usually controlled by decreasing the dose. Allergic or idiosyncratic reactions are rare, generally developing after one to four doses. Mild reactions are characterized by an urticarial or erythematous, maculopapular rash. Acute nonthrombocytopenic purpura with peripheral edema and fever, transient leukopenia, and a single case of fatal bullous dermatitis after administration of meprobamate and prednisolone have been reported. More severe and very

rare cases of hypersensitivity may produce fever, chills, fainting spells, angioneurotic edema, bronchial spasms, hypotensive crises (1 fatal case), anuria, anaphylaxis, stomatitis and proctitis. Treatment should be symptomatic in such cases, and the drug should not be reinstituted. Isolated cases of agranulocytosis, thrombocytopenic purpura, and a single fatal instance of aplastic anemia have been reported, but only when other drugs known to elicit these conditions were given concomitantly. Fast EEG activity has been reported, usually after excessive meprobamate dosage. Suicidal attempts may produce lethargy, stupor, ataxia, coma, shock, vasomotor and respiratory collapse.

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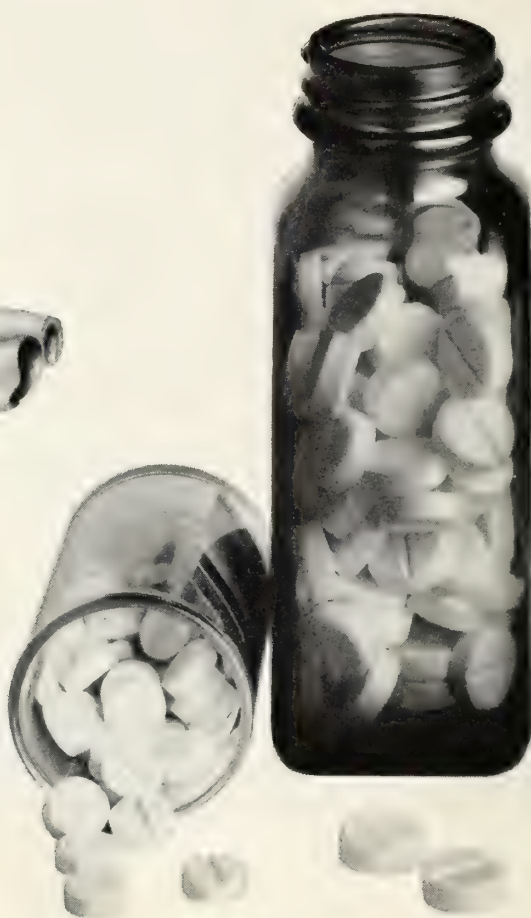
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The development of chlorothiazide and probenecid were events of major importance, but perhaps even more important for the future was the Renal Research Program by which they were developed. When Merck Sharp & Dohme organized this program in 1943, it was expressing in action some of its basic beliefs about research:

- Many problems connected with renal structure and function were still undefined or unsolved. The Renal Research Program would begin its basic research in some of these problem areas.

- From knowledge thus acquired might come clues to the development of new therapeutic agents of significant value to the physician.

For example, the Renal Research Program put fifteen years into this search before chlorothiazide became available. But because these years had first led to a greater understanding of basic problems, the desired criteria for chlorothiazide existed before the drug was developed.

Along with other research teams at Merck Sharp & Dohme, the Renal Research Program continues to add new understanding of basic problems—understanding which will lead to important new therapeutic agents.

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as affected by laser energy impacts revealed 17 per cent fewer cells in the lased samples. American culture exposed to the ruby laser beam showed clumping of the mitochondria which was however reversible after a time. HeLa cells were reduced by 11 per cent and if they were stained with green or blue dyes they became much more receptive to the absorption of laser energy. If the amount of energy was increased then disruption of the cell wall with extrusion of the cellular cytoplasm resulted.

Minton<sup>3</sup> reported permanent destruction by ruby and neodymium laser energy of the Cloudman S91 melanoma in the CDBA/2F<sub>1</sub> hybrid mouse. He developed a method of predicting the probability of permanent tumor destruction from the structure and absorption characteristics of the tumor; the size of the tumor, and the total amount of laser energy used.

At present a well regulated new-energy ruby laser system, sighted through an operating ophthalmoscope has been used for treatment of localized lesions of the eye such as retinal tears and certain tumors arising in the retina. Campbell, et al.<sup>4</sup> have described two or more retinal angiomas successfully treated by laser energy application. Amar<sup>5</sup> has treated two small retinal melanomas about 2 mm in diameter in two patients.

Helsper, et al.<sup>6</sup> succeeded in causing regression and eventual dissolution of small metastatic melanotic melanomas surgically exposed before laser therapy. Goldman and Wilson<sup>7</sup> previously reported cure of a basal-cell carcinoma of the right wrist and recently claimed apparent cure of a malignant melanoma about 1.5 cm in diameter on the right cheek of an 88 year old white male patient. There was no recurrence five months later. Reports of recent treatment of 4 basal-cell carcinomas, 2 Kaposi hemorrhagic sarcomas, 1 cavernous hemangioma and 1 tatoo in patients with high energy ruby laser radiation. Finally ruby laser radiation has been used during the course of a craniotomy for the removal of a brain tumor and the surrounding area.

McGuff, et al.<sup>1</sup> present a summary of four patients with malignant tumors that received laser energy. The first patient had melanotic melanoma. The tumor that received a full dose disappeared. A second lesion that received half a dose showed half disappearance of the tumor. The second patient with a recurrent squamous cell epithelioma of the antrum and orbit could not all be reached, and so it regressed but recurred slowly. A third patient with an intranasal melanoma was treated locally with only partial success because only about 10 per cent of the tumor was accessible to the laser energy. A fourth case with 4 subcutaneous mela-

notic melanomas were successfully treated after surgical exposure. The lesson from the reports is obvious: to cure a lesion, it must be made accessible to the laser beams. It is clear that unless all of the cancer is removed or destroyed to the last cell and does not recur over a period of years, the treatment is not curative and is ineffective.

It is clear that tumoricidal activity of laser energy depends on factors such as the absorption capability of the tumor, ratio of dose to tumor mass and the laser energy densities utilized. Deeper lesions of course require a surgical exposure for laser use unless they can be approached by means of modified endoscopes or redesigned fiber optic instruments. The experiments on cell cultures show that laser energy is unique because it has a selective effect upon certain malignant tumors in that it causes their progressive regression and eventual complete dissolution, while it causes only slight injury to normal tissue excluding the retina.

The mechanism of laser-energy action on certain malignant tumors is still unsolved. The thermal effects to be sure have been carefully observed, recorded and analyzed. However, the principle biologic effects of laser energy action on malignant tumors may be more than that of heat alone. Enzymes may be altered or lose their specificity. High electric fields may also cause the breaking of molecular bonds.

Greater investigation effort to determine the potential untoward effects of laser energy to the patient and operator must be made. An organized program of clinical investigation would be expedited by appropriate equipment and accurate energy output measurements.

L.H.N.

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## Walter Charleton And The Acceptance Of Epicurean Atomism In England

The revival of interest in Epicurean atomic theory in mid-seventeenth century England owed much to Robert Boyle. However, as Kargon points out in a recent essay,<sup>1</sup> it was a physician, Walter Charleton, who published the first presentation of the revived Epicurean atomism in England.

Walter Charleton was born in 1619 and died in 1707. He was educated at Magdalen Hall, Oxford. In 1643 he was appointed physician to Charles I, and in 1653 to Charles II in exile, although Charleton never left England. He was a fellow of the Royal Society and President of the Royal College of Physicians from 1689 to 1691. He also authored an important description of the lymphatics based on the work of George Joyliffe.<sup>2</sup>

The acceptance of Epicurean atomic theory at this time was hindered by its atheism. The concepts that motion is inherent in matter, that the soul is material and divisible, and that no Divine agent is required for the motion of atoms or the running of the universe were difficult to accept. In the struggle to reconcile the Platonic chain of being, the dualism of Descartes, and the emerging "natural philosophy" of science, the Cambridge platonists, particularly John Smith and Henry More, were critical of these antitheistic aspects of atomism in its Epicurean form. The main theological problem of the seventeenth century was the definition of God's power.<sup>3</sup> The Cambridge platonists approached these questions with quiet scholarship, and avoided the divisive and violent controversies of other religious thinkers of the time. Cartesian dualism went even too far for them, however, by raising the question of God's presence in his Creations, and the more conservative theologians believed in miracles and supernatural occurrences as a breach of natural laws.

Pierre Gassendi attempted to mitigate the atheism of Epicurus, Lucretius, and Democritus by conceding the necessity of God as the Agent of motion for atoms, and the indivisibility of the soul. His work was known in England, however, chiefly through the medium of scattered essays. The platonist criticism of both Cartesianism and Epicureanism was voiced by Henry More in 1654, in his "Antidote Against Atheism." In this he objected to the mechanical causation of motion and to explaining the universe without invoking Divine intervention. In the following year, Walter Charleton attempted to answer these objections in his "Physiologia Epicuro-Gassendo-Charltoniana." This was the first English attempt to establish atomism as an

acceptable philosophy. All physical phenomena are represented as taking place in absolute space and time. Matter consists of invisible atoms, created from nothing by God as the elements of the Universe, and imbued by Him with motion, the "First Cause of all Natural Actions." Atoms are not possessed of secondary qualities, but produce them by the effects of motion and of the shape and size of their aggregates. Heat is specifically related to speed of motion.

Charleton proceeds to point out that the differences between this view and ancient Greek atomism constitute a convincing proof of the existence of God. He considered it inconceivable that the complexities of the universe could arise as a consequence of pure chance, without the existence of a Divine Power.

Robert Boyle utilized both Cartesian and Epicurean concepts in experimental approaches, but his theory of matter, with occasional concessions to Descartes, is almost pure Epicureanism as modified by Gassendi and Charleton. Along with them, he maintained the role of God in the imparting of motion to the atom He created. Along with Charleton, Boyle found it impossible to accept the concept of God the Watchmaker, who made the universe, wound it up, and let it run. They postulated a continuing control by God of the motions and aggregations of the atoms, and of the course of the Universe He designed. Boyle differed from Gassendi and Charleton, however, in the view that space and time are absolute, uncreated, and independent of God; he required the addition of Divine influence here as well. Boyle's great influence in the acceptance of atomism in England can be attributed to his experimental successes and to the receptiveness of scholars at the time of his writings, somewhat later than those of Gassendi and Charleton.

In this seed time of scientific and philosophic ideas, Walter Charleton, physician to kings, played an important role in the development of science in England by reconciling the ancient mechanistic theory of the universe with the theology of his era.

H. L.

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BP reductions in the recumbent and sitting positions often are nearly as great as in the standing. In clinical trials, the average *recumbent* BP reduction was 36/18 mm. Hg.



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This was reflected in the relatively mild character of side effects seen in clinical trials (see below).

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# Prescribing information for **EUTRON**

**INDICATIONS:** Eutron (pargyline hydrochloride and methyclothiazide) is indicated in the treatment of patients with moderate to severe hypertension, especially those with severe diastolic hypertension. It is not recommended for use in patients with mild or labile hypertension amenable to therapy with sedatives and/or thiazide diuretics alone.

**CONTRAINDICATIONS:** Eutron is contraindicated in patients with pheochromocytoma, advanced renal disease, paranoid schizophrenia and hyperthyroidism. Until further experience is gained it cannot be recommended for use in patients with malignant hypertension, children (under 12 years of age), or pregnant patients.

The concomitant use of the following is contraindicated: other monoamine oxidase inhibitors; parenteral forms of reserpine or guanethidine; sympathomimetic drugs; foods high in tyramine such as cheese; imipramine and amitriptyline, or similar antidepressants; methyl dopa. A drug-free interval of two weeks should separate therapy and use of these agents.

**WARNINGS:** Pargyline hydrochloride is a monoamine oxidase inhibitor. Patients should be warned against eating cheese, and using alcohol, proprietary drugs or other medication without the knowledge of the physician. When it is necessary to administer alcohol, narcotics (notably meperidine), antihistamines, anesthetics, barbiturates and other hypnotics, sedatives, tranquilizers, or caffeine, these agents can be used cautiously at a dosage of  $\frac{1}{4}$  to  $\frac{1}{5}$  the usual amount. Avoid parenteral administration where possible. Withdraw pargyline two weeks before elective surgery.

Patients should be warned about the possibility of postural orthostatic hypotension. Those with angina or other evidence of coronary disease should not increase physical activity. Pargyline may lower blood sugar. Potassium depletion is unlikely at the recommended dosage, but if it occurs, adjust dosage or withdraw or provide added natural food sources of potassium; potassium tablets should be avoided wherever possible, as bleeding or obstructive ulceration of the small bowel has

been associated with their use; potassium levels should be especially watched if the patient is on digitalis or steroids, or if hepatic coma is impending.

**PRECAUTIONS:** When determining the anti-hypertensive effect of Eutron, blood pressure should be measured while the patient is *standing*. Use with caution in hyperactive or hyperexcitable persons. Such persons may show increased restlessness and agitation. Withdraw drug during acute febrile illness. Watch patients with impaired renal function for increasing drug effects or elevation of BUN and other evidence of progressive renal failure; withdraw drug if such alterations persist and progress. Pargyline has not been shown to cause damage to body organs or systems. As with all new drugs, complete blood counts, urinalyses, and liver function tests should be performed periodically. The drug should be used with caution in patients with liver dysfunction. With prolonged therapy, examine patients for change in color perception, visual fields, and fundi.

Elevated blood urea nitrogen, serum uric acid or blood sugar are possibilities attributable to the methyclothiazide in Eutron. Methyclothiazide may also reduce arterial response to pressor amines. Blood dyscrasias, including thrombocytopenia with purpura, agranulocytosis and aplastic anemia, have been seen with thiazide drugs.

**SIDE EFFECTS:** The use of pargyline may be associated with orthostatic hypotension. Mild constipation, slight edema, dry mouth, sweating, increased appetite, arthralgia, nausea and vomiting, headache, insomnia, difficulty in micturition, nightmares, impotence, delayed ejaculation, rash, and purpura have been encountered with pargyline. Hyperexcitability, increased neuromuscular activity (muscle twitching) and other extra-pyramidal symptoms have been reported. Drug fever is extremely rare. Congestive heart failure has been reported in a few patients with reduced cardiac reserve. Nocturia has been observed with the combination. If side effects persist, despite symptomatic therapy or reduction of the dose, discontinue the drug.



012214



# The Choice Of Systemic Antimicrobial Agents\*

■ Despite the availability of a variety of antimicrobial drugs effective against the same organisms, for each organism there is generally one drug, or occasionally a combination of drugs, which is likely to be more effective than other drugs of combinations. When bacterial resistance is encountered, or when the patient does not respond to or cannot tolerate a first-choice drug, there is usually a preferred order of choice among alternative drugs. For each organism, therefore, the accompanying table lists the antimicrobial agents of first choice and alternative agents in order of usual preference.

## Identification Of The Organism

The physician's first problem, of course, is identification of the organism responsible for the infection. The experienced clinician can sometimes correctly identify the organism on the basis of clinical evidence and without laboratory tests; in serious infections, however, bacteriologic smears, cultures and susceptibility tests are always necessary. The physician can perform some tests, such as Gram stain and simple cultures, in his own office; but whether he does the tests himself or entrusts them to a laboratory, the results should be interpreted with caution if they appear to conflict with the clinical evidence.

In acute pharyngitis, the Gram stain is of little value; accurate determination of the presence of beta-hemolytic Group A streptococci requires a culture. Many laboratories now use the fluorescent-tagged antibody (FA) technique, a reliable and rapid method for identifying Group A streptococci, enteropathogenic *E. coli*, *C. diphtheriae*, and gonococci. A Gram stain of unspun urine or exam-

ination of fresh, unstained urinary sediment is helpful in identifying urinary tract organisms. The best method for office identification of fungal infections is microscopic examination of skin scrapings or other material wet-mounted in 10% potassium hydroxide.

## Bacterial Susceptibility Tests

With some organisms, bacterial susceptibility tests are not necessary. Pneumococci and Group A streptococci, for example, are invariably susceptible to the penicillins. Susceptibility tests are, however, important in selecting drugs effective against organisms notorious for their inherent or developing resistance, such as the *Aerobacter-Klebsiella* groups, *Proteus*, *Pseudomonas*, *E. coli*, and staphylococci. The tests help show which drug is most likely to be useful against the infecting strain, and which second-choice drug should be tried if the first proves ineffective or the patient is not able to tolerate it.

The results of bacterial susceptibility tests appear to vary in different hospitals, even in the same community. Susceptibility tests are usually performed with prepared paper or plastic discs; zones of inhibition of an organism should be compared with those of a standard organism of the same species. Errors are especially frequent with sulfonamides. Disc susceptibility tests may give misleading information about enterococci, which are often resistant to both penicillin and streptomycin when tested singly, yet are uniformly susceptible to the combination. In endocarditis and other serious infections, many hospital laboratories use the tube-dilution method to provide more accurate quantitative information than can be obtained with discs.

An agent found active in susceptibility tests may prove ineffective in the patient for many reasons, including inadequate dosage, isolation and testing of an organism other than the one responsible for the infection, or the presence of undrained abscesses. Abscesses and empyema require surgical drainage; antibacterial agents alone can never be relied upon. Less often, an antimicrobial agent which is relatively inactive *in vitro* may prove effective in the patient. Thus, the activity of soluble sulfonamides, which can provide very high urine levels for the treatment of some acute urinary tract infections, may not be apparent from susceptibility tests. In no infection can susceptibility tests be accepted as a completely reliable guide; if the agent chosen on the basis of the tests appears to be in-

\* (NOTE: This special issue of the *Medical Letter* brings up to date material originally presented in the March 1, 1963 issue [Vol. 5, p. 17], as well as in the December 7, 1962 issue [Vol. 4, p. 97] on the identification of infecting organisms. Many of the recommendations have been changed to reflect both the introduction of new antimicrobial agents and more recent studies on the effectiveness and side effects of older agents. Recommendations for the treatment of some infrequently occurring infections have also been added. This issue should be used in conjunction with Issue 173 [Vol. 7, p. 69] entitled "Principal Toxic, Allergic and Other Adverse Effects of Antimicrobial Agents.")

effective, another may have to be substituted or a combination of two drugs may have to be used. In some severe infections or where resistant organisms are likely to be encountered (as in tuberculosis), combinations of antimicrobials may be used from the start.

After therapy is started, determination of the level of the antibacterial agent in the blood may be needed as a guide to safe and effective dosage, especially in patients with severe systemic infections, endocarditis, or renal insufficiency. In some infections, it is also important to re-culture the urine, blood or other material after the infection appears to have subsided, to determine whether the pathogen has been eliminated.

### **Severe Infections With Unidentified Organisms**

In such serious infections as meningitis and sepsis, and in some surgical infections, prompt treatment is essential, even when the responsible organism and its susceptibility to the various antimicrobial agents have not yet been determined. A Gram stain of appropriate secretions or excretions, such as sputum, urine, stool, wound exudate, and spinal fluid, often yields an early clue to the identity of the organism responsible for the infection, and provides a basis for choosing a drug for initial therapy before positive identification by other laboratory tests.

### **Initial Treatment Of Meningitis**

For the treatment of patients with purulent meningitis before the identity of the infecting organism has been determined, if the spinal fluid smear reveals cocci, either Gram-positive or Gram-negative, intravenous penicillin G in large doses (10 to 40 million units daily) should be administered. Cephalothin can be used in patients sensitive to penicillin. Some clinicians use an absorbable sulfonamide in addition, for its activity against meningococci, though several strains of meningococci are resistant to sulfonamides. If staphylococci are suspected, an antibiotic effective against penicillinase-producing staphylococci should be administered, along with penicillin G, until susceptibility tests have been completed. If the smear reveals Gram-negative bacilli, *H. influenzae* should be suspected, and treatment with chloramphenicol (with or without streptomycin) is favored by several Medical Letter consultants.

The drugs used against meningitis should generally be administered intravenously to insure maximum penetration of the blood-brain barrier. Although a few clinicians favor combined intravenous-intrathecal therapy for all bacterial meningitis, most Medical Letter consultants favor com-

bined intravenous-intrathecal administration only when polymyxin B is to be used for the treatment of suspected *Pseudomonas meningitis*; the toxicity of this drug precludes the use of sufficiently large doses for the maintenance of adequate spinal fluid levels when it is administered only by the intravenous route.

If the organism causing meningitis cannot be classified or tentatively identified from examination of a smear of the first spinal tap, initial treatment pending identification by culture should be based on the knowledge that in the new-born, coliform or other enteric bacilli are most likely to be responsible; beyond three months and up to about age five, most meningeal infections are caused by *H. influenzae*; in older children and in adults, pneumococci and meningococci are the organisms most frequently responsible for meningitis.

### **Initial Treatment Of Sepsis**

Medical Letter consultants differ as to the choice of drugs for initial emergency treatment of suspected severe bacterial sepsis before the responsible organism has been identified. The choice of drugs should be based on probable source of infection (such as the genitourinary tract); but should also to a considerable extent reflect the changing patterns of bacterial resistance seen in the community and the hospital. In infections acquired in a hospital, postoperative, or otherwise, a resistant staphylococcus is often the responsible organism, and, pending laboratory studies, one of the antibiotics effective against resistant staphylococci should be used.

On the basis of clinical experience during the past year, several Medical Letter consultants prefer cephalothin for initial treatment of *suspected* bacterial sepsis, pending laboratory studies, because of its bactericidal activity against many organisms, including penicillinase-producing staphylococci; its choice is especially indicated when renal insufficiency precludes the use of other bactericidal drugs, such as kanamycin, neomycin and vancomycin. Gram-negative bacterial sepsis is often a superinfection or complication of previous antimicrobial therapy; it is important to obtain a history of previous therapy and to avoid the administration of recently used agents.

### **Urinary Tract Infections**

For effective treatment of urinary tract infections, a high level of the antimicrobial agent in the urine is desirable, though no antimicrobial agent can cure urinary tract infections until obstruction or other causes of stasis of urine are remedied. Oral administration of an absorbable sulfonamide, such as Trisulfapyrimidines USP or Sulfisoxazole USP, is often effective in acute infections. Nitrofurantoin



and methenamine mandelate act mainly as urinary antiseptics with little if any tissue penetration. In chronic or recurrent urinary tract infections, especially those associated with sepsis or fever, an antibacterial agent that produces adequate blood and tissue levels as well as high urine levels is usually preferred. In some chronic infections, however, a combination of methenamine mandelate and an acidifying agent may prove effective; bacteria rarely develop resistance to methenamine mandelate. When renal insufficiency is associated with a urinary tract infection, ampicillin can be tried first in patients not sensitive to penicillin; in adequate doses, it produces high urine and blood levels without toxicity.

### Prophylaxis

There are few indications for the prophylactic use of antimicrobial drugs. Antimicrobial prophylaxis is recommended against epidemic meningococcal infections, rheumatic fever, subacute bacterial endocarditis, chronic bronchitis, and pulmonary tuberculosis; it is also recommended for patients with severe contaminated wounds. The value of sulfonamides for prophylaxis against meningococcal meningitis is now questionable because of the appearance of resistant strains. Prophylactic use of

antibiotics has not been shown to prevent bacterial complications of acute viral respiratory disease.

### Administration And Dosage

When an antimicrobial agent is available in both oral and parenteral forms, parenteral administration, preferably intravenous, generally is mandatory if the infection is severe, or if there is nausea and vomiting. When oral penicillins are used, it should be remembered that even with those resistant to gastric acid, absorption is usually greatest when they are taken on an empty stomach. Such potentially irritating drugs as tetracycline, erythromycin and nitrofurantoin are best given with food.

In general, the dosage, frequency and duration of treatment with any agent, but especially the more toxic agents, should take into account not only the severity of the disease, but also the state of renal, hepatic and hematopoietic function. Urinary excretion is the main route of elimination of most antimicrobial agents, and severely impaired excretion may result in dangerously high concentrations in the blood and tissues unless reduced doses are given. Newborn infants present special problems in drug metabolism and renal excretion which require marked reduction of dosage with many drugs, especially with chloramphenicol and the sulfonamides.

| INFECTING ORGANISM                                    | DRUG OF FIRST CHOICE                                                | ALTERNATIVE DRUGS                                                                    |
|-------------------------------------------------------|---------------------------------------------------------------------|--------------------------------------------------------------------------------------|
| <b>Gram-positive cocci</b>                            |                                                                     |                                                                                      |
| Streptococcus pyogenes<br>groups A, B, C and G        | a penicillin <sup>1</sup>                                           | erythromycin; cephalothin                                                            |
| *Streptococcus viridans                               | a penicillin <sup>1</sup> with or without streptomycin <sup>2</sup> | cephalothin                                                                          |
| *Enterococcus                                         | a penicillin <sup>1</sup> with streptomycin <sup>2</sup>            | erythromycin or cephalothin with streptomycin <sup>2</sup> ; ampicillin <sup>1</sup> |
| *Streptococcus anaerobius                             | a tetracycline <sup>2,3</sup>                                       | a penicillin <sup>1</sup>                                                            |
| Pneumococcus                                          | a penicillin <sup>1</sup>                                           | erythromycin; cephalothin                                                            |
| *Staphylococcus aureus<br>non-penicillinase-producing | a penicillin <sup>1</sup>                                           | erythromycin; cephalothin                                                            |
| penicillinase-producing                               | a penicillinase-resistant penicillin <sup>4</sup>                   | cephalothin; lincomycin; vancomycin <sup>2</sup>                                     |
| <b>Gram-negative cocci</b>                            |                                                                     |                                                                                      |
| Meningococcus                                         | a penicillin <sup>1</sup>                                           | a sulfonamide <sup>5,6</sup> ; ampicillin <sup>1</sup> ; cephalothin; erythromycin   |
| Gonococcus                                            | a penicillin <sup>1</sup>                                           | erythromycin; cephalothin; a tetracycline <sup>2,3</sup>                             |
| <b>Gram-positive bacilli</b>                          |                                                                     |                                                                                      |
| Bacillus anthracis (anthrax)                          | a penicillin <sup>1</sup>                                           | erythromycin; a tetracycline <sup>2,3</sup>                                          |
| Listeria monocytogenes                                | a penicillin <sup>1</sup>                                           | erythromycin; a tetracycline <sup>2,3</sup>                                          |
| Clostridium tetani <sup>7</sup>                       | a penicillin <sup>1</sup>                                           | a tetracycline <sup>2,3</sup>                                                        |
| Clostridium welchii (gas gangrene) <sup>8</sup>       | a penicillin <sup>1</sup> with or without streptomycin <sup>2</sup> | a tetracycline <sup>2,3</sup> with or without streptomycin <sup>2</sup>              |
| Corynebacterium diphtheriae <sup>9</sup>              | a penicillin <sup>1</sup>                                           | erythromycin; cephalothin                                                            |

\* Bacterial susceptibility tests are usually essential.

**Gram-negative bacilli**

|                                                                   |                                                                               |                                                                                                                                    |
|-------------------------------------------------------------------|-------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------|
| *Salmonella <sup>10</sup>                                         | chloramphenicol <sup>2</sup>                                                  | ampicillin <sup>1</sup> ; cephalothin                                                                                              |
| *Shigella <sup>11</sup>                                           | ampicillin <sup>1</sup>                                                       | kanamycin (oral) or neomycin (oral);<br>a tetracycline <sup>2,3</sup> ; cephalothin;<br>chloramphenicol <sup>2</sup>               |
| *Escherichia coli<br>enteropathogenic                             | kanamycin (oral) or neomycin<br>(oral)                                        | ampicillin <sup>1</sup> ; a tetracycline <sup>2,3</sup>                                                                            |
| sepsis                                                            | kanamycin (parenteral) <sup>2</sup> or<br>neomycin (parenteral) <sup>2</sup>  | chloramphenicol <sup>2</sup> ; a tetracycline <sup>2,3</sup><br>polymyxin B <sup>2</sup> or colistimethate <sup>2</sup>            |
| urinary infections                                                | a sulfonamide <sup>12</sup>                                                   | ampicillin <sup>1</sup> ; a tetracycline <sup>2,3</sup><br>nitrofurantoin <sup>2,13</sup> ; methenamine<br>mandelate <sup>13</sup> |
| *Aerobacter aerogenes                                             | a tetracycline <sup>2,3</sup> with or without<br>streptomycin <sup>2,14</sup> | chloramphenicol <sup>2</sup> with or without<br>streptomycin <sup>2,14</sup> ; cephalothin                                         |
| *Klebsiella pneumoniae                                            | a tetracycline <sup>2,3</sup> with or without<br>streptomycin <sup>2,14</sup> | cephalothin; chloramphenicol <sup>2</sup> with or<br>without streptomycin <sup>2,14</sup> ; kanamycin <sup>2</sup>                 |
| *Proteus mirabilis <sup>15</sup>                                  | a penicillin <sup>1</sup>                                                     | cephalothin; chloramphenicol <sup>2</sup>                                                                                          |
| *other Proteus                                                    | chloramphenicol <sup>2</sup> with or without<br>streptomycin <sup>2,14</sup>  | kanamycin <sup>2</sup> ; a tetracycline <sup>2,3</sup> with or<br>without streptomycin <sup>2,14</sup>                             |
| *Pseudomonas aeruginosa                                           | polymyxin B <sup>2</sup> or colistimethate <sup>2</sup>                       | no dependable alternative                                                                                                          |
| *Brucella                                                         | a tetracycline <sup>2,3</sup> with or without<br>streptomycin <sup>2,14</sup> | chloramphenicol <sup>2</sup> with or without<br>streptomycin <sup>2,14</sup>                                                       |
| Pasteurella tularensis                                            | streptomycin <sup>2</sup>                                                     | a tetracycline <sup>2,3</sup> chloramphenicol <sup>2</sup>                                                                         |
| Pasteurella pestis (bubonic<br>plague)                            | streptomycin <sup>2</sup> with or without<br>a sulfonamide <sup>6</sup>       | a tetracycline <sup>2,3</sup> chloramphenicol <sup>2</sup>                                                                         |
| Hemophilus influenzae<br>respiratory infections                   | ampicillin <sup>1</sup>                                                       | a tetracycline <sup>2,3</sup>                                                                                                      |
| meningitis                                                        | chloramphenicol <sup>2</sup> with or without<br>streptomycin <sup>2</sup>     | a tetracycline <sup>2,3</sup> with or without<br>streptomycin <sup>2</sup> ; ampicillin <sup>1</sup>                               |
| Bacteroides                                                       | a tetracycline <sup>2,3</sup>                                                 | a penicillin <sup>1</sup> ; chloramphenicol <sup>2</sup>                                                                           |
| Hemophilus ducreyi (chancroid)                                    | a tetracycline <sup>2,3</sup>                                                 | a sulfonamide; chloramphenicol <sup>2</sup> ;<br>streptomycin <sup>2</sup>                                                         |
| Streptobacillus moniliformis<br>(rat bite fever; Haverhill fever) | a penicillin <sup>1</sup>                                                     | erythromycin; streptomycin <sup>2</sup>                                                                                            |
| Bordetella pertussis                                              | ampicillin <sup>1</sup>                                                       | a tetracycline <sup>2,3</sup>                                                                                                      |
| *Mima-Herellea                                                    | a penicillin <sup>1</sup>                                                     | kanamycin <sup>2</sup> ; polymyxin B <sup>2</sup> or<br>colistimethate <sup>2</sup>                                                |
| Fusobacterium (Vincent's<br>infection)                            | a penicillin <sup>1</sup>                                                     | a tetracycline <sup>2,3</sup> ; erythromycin                                                                                       |
| Actinobacillus mallei (glanders)                                  | streptomycin <sup>2</sup> plus a tetracycline <sup>2,3</sup>                  | streptomycin <sup>2</sup> plus a sulfonamide <sup>6</sup>                                                                          |
| Malleomyces pseudomallei<br>(melioidosis)                         | streptomycin <sup>2</sup> plus a tetracycline <sup>2,3</sup>                  | streptomycin <sup>2</sup> plus a sulfonamide <sup>6</sup>                                                                          |
| Donovania granulomatis<br>(granuloma inguinale)                   | a tetracycline <sup>2,3</sup>                                                 | chloramphenicol <sup>2</sup> ; streptomycin <sup>2</sup>                                                                           |
| Vibrio comma (cholera) <sup>16</sup>                              | a tetracycline <sup>2,3</sup>                                                 | chloramphenicol <sup>2</sup> ; streptomycin <sup>2</sup>                                                                           |

1. Potassium penicillin G, penicillin V, phenethicillin and ampicillin can be used for oral treatment of infections by non-penicillinase-producing staphylococci and other Gram-positive and Gram-negative cocci. Ampicillin is also effective against many Gram-negative bacilli. Although penicillin G is less resistant to degradation by gastric acid than penicillin V, phenethicillin, or ampicillin, the amount absorbed is generally adequate if it is taken on an empty stomach; in fact, absorption of any oral penicillin is likely to be more rapid and complete if it is taken on an empty stomach (at least three hours after a meal), when gastric acidity is relatively low. For severe infections by non-penicillinase-producing staphylococci and other susceptible organisms, potassium penicillin G should

be administered parenterally. Procaine penicillin G aqueous, an intramuscular penicillin, can be administered once or twice daily in less severe infections caused by organisms susceptible to penicillin G. Benzathine penicillin G, a longer-acting intramuscular preparation which is also active against such organisms, is used at intervals as long as a week or 10 days for treatment, and as long as a month for prophylaxis against rheumatic fever. Allergic reactions to all penicillins are common. An allergic reaction to one penicillin usually means that it will occur with the others.

2. Capable of causing severe adverse effects. See The Medical Letter, Vol. 7, pp. 69-72, Aug. 27, 1965, and manufacturer's package inserts for precautions and contraindications.



| INFECTING ORGANISM                                                              | DRUG OF FIRST CHOICE                                                               | ALTERNATIVE DRUGS                                                                                       |
|---------------------------------------------------------------------------------|------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------|
| <b><i>Acid-fast bacilli</i></b>                                                 |                                                                                    |                                                                                                         |
| * <i>Mycobacterium tuberculosis</i> <sup>17</sup>                               | isoniazid plus p-aminosalicylic acid and streptomycin <sup>2</sup>                 | cycloserine <sup>2</sup> ; viomycin <sup>2</sup> ; pyrazinamide <sup>2</sup> ; ethionamide <sup>2</sup> |
| *Atypical mycobacteria <sup>18</sup><br><i>Mycobacterium leprae</i> (leprosy)   | ethionamide <sup>2</sup><br>sulfones <sup>2, 19</sup>                              | erythromycin; streptomycin <sup>2</sup><br>amithiozone <sup>2</sup>                                     |
| <b><i>Spirochetes</i></b>                                                       |                                                                                    |                                                                                                         |
| <i>Spirillum minus</i> (rat bite fever)                                         | a penicillin <sup>1</sup>                                                          | erythromycin; streptomycin <sup>2</sup>                                                                 |
| <i>Borrelia recurrentis</i> (relapsing fever)                                   | a tetracycline <sup>2, 3</sup>                                                     | chloramphenicol <sup>2</sup> ; a penicillin <sup>1</sup>                                                |
| <i>Treponema pallidum</i>                                                       | a penicillin <sup>1</sup>                                                          | erythromycin; a tetracycline <sup>2, 3</sup>                                                            |
| <i>Treponema pertenue</i> (yaws)                                                | a penicillin <sup>1</sup>                                                          | erythromycin; a tetracycline <sup>2, 3</sup>                                                            |
| <i>Leptospira</i>                                                               | a penicillin <sup>1</sup>                                                          | a tetracycline <sup>2, 3</sup>                                                                          |
| <b><i>Rickettsia</i></b> Rocky Mountain spotted fever, endemic typhus, Q fever) |                                                                                    |                                                                                                         |
|                                                                                 | a tetracycline <sup>2, 3</sup>                                                     | chloramphenicol <sup>2</sup>                                                                            |
| <b><i>Viruses</i></b>                                                           |                                                                                    |                                                                                                         |
| <i>Mycoplasma</i> (atypical viral pneumonia)                                    | a tetracycline <sup>2, 3</sup>                                                     | chloramphenicol <sup>2</sup>                                                                            |
| Psittacosis                                                                     | a tetracycline <sup>2, 3</sup>                                                     | chloramphenicol <sup>2</sup>                                                                            |
| Lymphogranuloma venereum                                                        | a tetracycline <sup>2, 3</sup>                                                     | chloramphenicol <sup>2</sup> ; a sulfonamide <sup>6</sup>                                               |
| Vaccinia                                                                        | vaccinia immune globulin with or without methisazone                               | no alternative                                                                                          |
| Herpetic keratitis                                                              | idoxuridine (topical)                                                              | no alternative                                                                                          |
| Trachoma                                                                        | oral or topical tetracycline <sup>2, 3</sup> plus an oral sulfonamide <sup>6</sup> | chloramphenicol (topical)                                                                               |
| Inclusion conjunctivitis                                                        | oral or topical tetracycline <sup>2, 3</sup>                                       | chloramphenicol (topical)                                                                               |

- Any one of the tetracycline group of antibiotics can be used (chlortetracycline, demethylchlortetracycline, oxytetracycline or tetracycline hydrochloride).
- For oral treatment of penicillinase-producing staphylococci, nafcillin, cloxacillin or oxacillin can be used. For severe infections, a parental formulation (methicillin, oxacillin or nafcillin) should be used.
- Because of the appearance of sulfonamide-resistant strains, a sulfonamide can no longer be considered the drug of first choice for either prophylaxis or therapy of meningococcal meningitis.
- For parenteral administration, Sodium Sulfadiazine Injection USP can be used. For oral administration, an absorbable sulfonamide, such as Trisulfapyrimidines USP or Sulfadiazine USP, should be used. Long-acting formulations should not be used.
- Proper debridement and a fluid toxoid booster dose are primary; if there has been no previous toxoid immunization, tetanus immune globulin (human) in doses of at least 3000 units should be administered. Clinicians disagree as to the value of penicillin alone in the treatment of tetanus.
- Debridement is primary; value of antitoxin is not certain; large doses (at least 10 million units daily) of penicillin G are required.
- Antitoxin is primary; antibiotics only for carrier state or as adjuncts to antitoxin.
- Chloramphenicol is the first choice for typhoid fever; ampicillin is first choice for other *Salmonella* infections; most cases of *Salmonella* infection subside spontaneously.
- Many, if not most, strains are resistant to sulfonamides, formerly the drugs of choice.
- For an uncomplicated first episode of lower urinary tract infection with *E. coli* or other urinary pathogens, the drug of first choice is one of the soluble sulfonamides, such as Sulfisoxazole USP, Trisulfapyrimidines USP, sulfisomidine or sulfamethizole (but not a long-acting sulfonamide). If after 48 hours there is no improvement, either in symptoms or in urine culture, or if the urinary tract infection is chronic, recurrent or severe, susceptibility tests should be used to select an effective drug.
- For antibacterial action in urine; little, if any, penetration into tissues; not suitable for systemic infections.
- Streptomycin is usually included for the treatment of severe infections.
- Penicillin G and ampicillin are the drugs of first choice in the treatment of *Proteus mirabilis* infections, but large doses of penicillin G (10 to 40 million units daily) or of ampicillin (6 Gm, or more, daily) are necessary. Many strains of *Proteus* other than *mirabilis* are resistant to some of the drugs listed; susceptibility tests are necessary.
- Prompt replacement of fluids and electrolytes is essential.
- For treatment of tuberculosis, a combination of drugs is preferred.
- Most atypical mycobacteria are resistant to isoniazid and p-aminosalicylic acid.
- Acetosulfone, dapsone, sulfoxone sodium or glucosulfone sodium.
- Amphotericin B (parenteral) is first choice for sepsis, pneumonia, meningitis, and other systemic infections; where topical therapy is indicated, as in enteric infections; nystatin is preferable to amphotericin B.
- Griseofulvin should be used when topical drugs are ineffective.

| INFECTING ORGANISM            | DRUG OF FIRST CHOICE                                                   | ALTERNATE DRUGS                                                                             |
|-------------------------------|------------------------------------------------------------------------|---------------------------------------------------------------------------------------------|
| <b>Fungi</b>                  |                                                                        |                                                                                             |
| Actinomyces                   | a penicillin <sup>1</sup>                                              | a tetracycline <sup>2,3</sup> ; cephalothin;<br>chloramphenicol <sup>2</sup>                |
| Nocardia                      | a sulfonamide <sup>6</sup> with or without<br>cycloserine <sup>2</sup> | a tetracycline <sup>2,3</sup> ; chloramphenicol <sup>2</sup> ;<br>streptomycin <sup>2</sup> |
| Histoplasma capsulatum        | amphotericin B <sup>2,20</sup>                                         | a sulfonamide <sup>6</sup>                                                                  |
| Candida albicans              | nystatin (topical)                                                     | amphotericin B <sup>2,20</sup>                                                              |
| Aspergillus                   | amphotericin B <sup>2,20</sup>                                         | no dependable alternative                                                                   |
| Cryptococcus neoformans       | amphotericin B <sup>2,20</sup>                                         | no dependable alternative                                                                   |
| Mucor                         | amphotericin B <sup>2,20</sup>                                         | no dependable alternative                                                                   |
| Coccidioides immitis          | amphotericin B <sup>2,20</sup>                                         | no dependable alternative                                                                   |
| Blastomyces                   | amphotericin B <sup>2,20</sup>                                         | 2-hydroxystilbamidine <sup>2</sup>                                                          |
| Sporotrichum schenckii        | iodides                                                                | amphotericin B <sup>2,20</sup>                                                              |
| Dermatophytoses (Tinea, etc.) | griseofulvin <sup>21</sup>                                             | no alternative systemic drug                                                                |

#### PARTIAL LIST OF BRAND NAMES

|                                                                                                                  |                                                                          |
|------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------|
| Acetosulfone—Promacetin (Parke, Davis)                                                                           | Methicillin—Staphicillin (Bristol); Dimocillin-RT (Squibb)               |
| Amphotericin B—Fungizone (Squibb)                                                                                | Methisazone—Marboran (Borroughs Wellcome)                                |
| Ampicillin—Penbritin (Ayerst); Polycillin (Bristol)                                                              | Nafcillin—Unipen (Wyeth)                                                 |
| Cephalothin—Keflin (Lilly)                                                                                       | Nitrofurantoin—Furadantin—Eaton)                                         |
| Chloramphenicol—Chloromycetin (Parke, Davis)                                                                     | Nystatin—Mycostatin (Squibb)                                             |
| Chlortetracycline—Aureomycin (Lederle)                                                                           | Oxacillin—Prostaphlin (Bristol); Resistopen (Squibb)                     |
| Cloxacillin—TegoPen (Bristol)                                                                                    | Oxytetracycline—Terramycin (Pfizer)                                      |
| Colistimethate (polymyxin E)—Coly-Mycin (Warner, Chilcott)                                                       | Penicillin G (benzathine)—Bicillin (Wyeth)                               |
| Cycloserine—Seromycin (Lilly)                                                                                    | Penicillin G (potassium—many manufacturers)                              |
| Dapsone—Avlosulfon (Ayerst)                                                                                      | Penicillin V—Compcillin-V (Abbott); V-Cillin (Lilly);<br>Pen-Vee (Wyeth) |
| Demethylchlortetracycline—Declomycin (Lederle)                                                                   | Phenethicillin—Syncillin (Bristol; and others)                           |
| Erythromycin—Erythrocin (Abbott); Ilosone (Lilly); Ilotycon<br>(Lilly); Pediamycin (Ross); Erythromycin (Upjohn) | Polymyxin B—Aerosporin (Burroughs Wellcome)                              |
| Ethionamide—Trecator (Ives)                                                                                      | Pyrazinamide—Pyrazinamide (Merck)                                        |
| Glucosulfone—Promin (Parke, Davis)                                                                               | Sulfamethizole—Thiosulfil (Ayerst; and others)                           |
| Griseofulvin—Grisactin (Ayerst); Grifulvin V (McNeil);<br>Fulvicin-U/F (Schering)                                | Sulfisoxazole—Gantrisin (Roche; and others)                              |
| Kanamycin—Kantrex (Bristol)                                                                                      | Sulfoxone—Diasone Sodium (Abbott)                                        |
| Lincomycin—Lincocin (Upjohn)                                                                                     | Tetracycline HCl—Achromycin (Lederle; and others)                        |
| Methenamine mandelate—Mandelamine (Warner, Chilcott)                                                             | Vancomycin—Vancocin (Lilly)                                              |
|                                                                                                                  | Viomycin—Vinactane (Ciba); Viomycin (Parke, Davis);<br>Viocin (Pfizer)   |

#### THE ANESTHETIST'S OPPORTUNITY

The anesthetist has an extraordinary opportunity to study the effects of certain drugs and procedures in man. He must, of course, go into the animal laboratory from time to time to test certain agents or procedures, but animals are primarily in the domain of the "basic" pharmacologist or physiologist. There is no need for the anesthetist to compete disadvantageously in their realm. The anesthetist can take advantage of his remarkable possibilities—in the main denied to the "basic" scientists—for studying human physiology and human pharmacology. This privilege brings with it heavy responsibilities, heavy ethical problems.

—Beecher, H. K.: Anesthetist as Investigator, *Anesthesiology* 25: 445-453 (July) 1964.



# Review And Grievance Committees

J. Alfred Fabro, M.D.

■ One of the most common causes of difficulty between physicians and patients is fees.<sup>1</sup> To handle such problems The American Medical Association has recommended the creation and use of Review and Grievance Committees. It further recommends that they be incorporated into the Bylaws of the various associations.

The need for and use of such committees will be increased by the recent enactment of the Medicare Bill and the expansion of Major Medical Insurance plans. Because there is some confusion about the differences between the two committees, and from committees on Ethics and Discipline, I shall present a brief summary from authoritative sources explaining their functions.

## Grievance Committees

In 1949, the House of Delegates of the AMA adopted a resolution recommending that all constituent associations establish Grievance Committees.

In 1954, the Board of Trustees of the AMA, acting on a resolution of the House of Delegates, appointed a committee to study and clarify the functions of Grievance Committees. It published its report as "Guides for Medical Society Grievance Committees."<sup>2</sup>

"The purposes of Grievance Committees are to prevent and resolve misunderstandings, to clarify and adjust differences between physician and patient, and to assist in maintaining the high levels of professional deportment already established by the Principles of Medical Ethics.

"Grievance Committees should be empowered . . . with authority to receive complaints, to investigate, mediate, arbitrate, and, where necessary, refer them to appropriate bodies for adjudication."

The Report notes the variety of names given such a committee acting vis-à-vis the public, but it concludes that "Grievance Committee" is "unquestionably" the name most realistic and the best understood by the profession and the public. Basically, the Grievance Committee is a non-disciplinary committee acting to resolve complaints between patients or third parties and physicians.

To emphasize its value, the AMA states: "Grievance Committee is of such compelling importance in modern medical organization that a special committee, uniformly designated to disclose unmistakably its true function, should be created and main-

tained by every constituent association for this purpose and this purpose only."

The Guide recommends that bylaws of associations include provisions clearly stating the purpose, extent of authority, and duties of the committee.

It recommends broad representation on the committee, with overlapping terms. ". . . members [of Grievance Committees] should not serve simultaneously on any disciplinary or appeal body."

"Discipline is not a proper function of a Grievance Committee under any circumstances. Where a Grievance Committee finds that disciplinary measures are indicated, it should recommend to the appropriate judicial body."

It further recommends that there be no limitation upon the source of a complaint so long as it is responsible.

Grievance Committees can also act to initiate investigations. The complainee of course should be guaranteed certain rights so that he can properly prepare an answer. But he is not on trial. "The Grievance Committee is never to act as a trial body or to effect discipline."

The Guide advises preservation of a record of its proceedings. Reports also should be made to the governing body.

As to publicity: "The establishment of Grievance Committees is a service of medical organizations to the public, but this service cannot succeed unless the public knows of its existence and understands how to use it . . . The method of operation of these committees should be continuously publicized through legitimate channels of lay communication."

## Review Committees

Of late there has been an increase in the use of the Review Committee by medical associations. The particular need for and impetus to Review Committees is the growth of Major Medical plans and the recent enactment of Medicare. Major medical plans differ in detail, but most have a deductible feature (e.g. \$500.), paying a percentage (e.g. 80 per cent) over the deductible amount of all ex-

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penses of an illness up to a maximum (e.g. \$10,000.). The physician is reimbursed not from a fee schedule (as Blue Shield) but is paid the "usual and customary" fee for such a medical service in the area.

To define and differentiate it from the Grievance Committee, we summarize "A Report on Medical Society Review Committees in the U. S.,"<sup>3</sup> a study by the Health Insurance Council which represents the insurance industry.

"It is the primary purpose of such committees to provide impartial professional advice with respect to fees charged by physicians which appear to vary from what is customary or normal.

"A review committee does not have legal, judicial, or punitive powers and in no way does it function as a grievance committee or as a forum to hear complaints. It serves only as a fact-finding, advisory, and educational medium through which insurers, physicians, and patients can communicate.

"The prime objective of the review committee is to provide a forum for reconciling the concept of usual and customary fees under major medical type coverages with the charging practices of the medical profession in a given area."

Because the word "grievance" connotes discipline to some, the insurance industry, fortified by the Report of the Commission on the Cost of Medical Care adopted by the AMA delegates in December 1964, prefers and urges the adoption of the Review Committee. It functions only for guidance and information—to suggest what is the "usual and customary" fee in the community in which the service is rendered. This committee is used mostly by the insurance industry, especially relative to Major Medical plans. They emphatically state that such requests are not to be considered as complaints.

The majority of review committees have been established since 1959, increasing with the growth of major medical expense insurance. Medicare may provide an impetus to creation of such committees where none exists.

It is admitted and accepted that the fee is a contract between the physician and patient. The Major Medical is a contract between insurer and patient whereby the insurer is obligated to pay "the usual and customary" fee. Any amount above this becomes the patient's responsibility to his physician.

The difficulty arises in defining and quantitating "usual and customary" fees for "reasonable and necessary" services. The health industry did not feel competent to set such fees, so it has sought help from organized medicine when questions and problems arose. But it does not like to use the grievance committee; "Grievance" has, for it, a connotation of disciplinary action. It did not wish its request for information and guidance to be interpreted as

a complaint. "Review" satisfies their conception of the problem.

The Report of the AMA Commission on the Cost of Medical Care, adopted by AMA House of Delegates in December 1964, also underscored the distinction between grievance and review committees, between a complaint and a request for information. It states that "the fundamental advantage a review committee has over the grievance committee is that such a committee is known as an advisory mechanism without the implication of immediate disciplinary action."

As of August 1964, 33 state societies had review committees. There are also many county and city review committees.

The insurance industry recommends and provides technical assistance to the committees. Believing that such committees are educational to physicians, the public, and to insurance personnel, it recommends that insurance personnel be included in such committees without vote, to provide information and technical assistance, as well as for their own edification.

In October 1962, the Health Insurance Council, after studying existing review committees, issued a guide including desirable features and procedures. Among them were:

1. Insurers utilize any guides or criteria for fees provided by medical societies.
2. Try to resolve any problem with the physician before using the committee.
3. Review Committees adopt a short form, requesting pertinent, factual information only.
4. Insurance personnel serve the committees as consultants "but in no event represent a company submitting a case or be a member of the committee."
5. The review committee be willing to support its opinion before any grievance committee.

From the Health Council's study of existing review committees, though no two are alike, certain generalizations can be made.

1. Some committees accept problems from physicians as well as from patients.
2. The majority of committees have not accepted the principle of insurance company representation. Where accepted, such personnel act as consultants on a non-voting basis, or are present by invitation.
3. All committees require the insurer to discuss the case with the physicians first.
4. Practically no medical societies have a published schedule of "usual" or "customary" charges. Insuring companies probably use Blue Shield or Relative Value to decide whether or not a fee should be questioned."



5. A majority of committees provide an appeal mechanism to their opinion.

The criteria to determine "usual and customary" fees vary. Factors considered are:

1. Family income.
2. Type and complexity of procedure.
3. Standing of the physician. In Philadelphia, for example, professors command higher fees.
4. Skill and competence of the physician.
5. Type of hospital accommodation.

Most functioning committees feel they must consult with the physician about the questioned fee. But they agree that their function is only to set "usual and customary" fees; this represents the insurer's liability. Any amount above this is the patient-insured's responsibility to his physician; the physician's responsibility being to justify the differential to the patient, who is responsible for any amount above the "usual and customary" fee.

In the Miami area the Committee uses as "usual and customary" that fee charged for a particular procedure in the area by doctors of comparable specialty and experience as the doctor rendering the service to patients of income status similar to that of the patient receiving the services."

In 148 cases reviewed by the Massachusetts committee, it recommended reduction of fee in 97 cases, while in 51 the physician's charge was upheld. The total reduced in the 97 cases was \$97,000.

In New York County, of 182 cases, 97 were reduced; 85 were upheld. The total reduced was \$64,344. The committee reduced 68 of the 97 because of the income of the insured.

Some review committees have received requests from insurers to review hospital utilization. Though such problems are more properly handled by hospital Utilization Committees, it was felt that the matter might be referred to a review committee if the hospital failed to review such cases or gave an unsatisfactory reply to an insurer's request.

The insurance business and the AMA believe that such committees are beneficial and educational to both physicians and insurance personnel and will help preserve the voluntary health insurance principle.

These brief summaries reveal differences between the two committees, but there still are valid questions. Is there a necessary division between the two? Even if the committees were designated as a separate Review and Grievance Committee, could not the personnel be the same, care being used to differentiate their functions and procedure? Is the review committee actually a euphemism for grievance committee?

What do we do in Connecticut? The Bylaws of the Connecticut State Medical Society have no provision for them. The Fairfield County has incorpo-

rated a provision in its Bylaws for the formation of a Review Committee. The Hartford County Society has utilized when needed an ad hoc Review Committee as a subcommittee of its Board of Directors—not included in its Bylaws. No other county association in Connecticut has included any provision of either a Review or Grievance Committee in its Bylaws. Such problems are handled under their committee on discipline or ethics.

Fairfield County Medical Society: Recently it has included in its Bylaws a "Review Committee" as a standing committee.

#### *"Review Committee"*

"Par. 1. Inquiries and complaints directed to the Association against a member solely in regard to fees shall be referred to the Review Committee. Matters involving fees but basically involving the method or ethics of medical practice shall be referred to the Board of Censors for action.

"Par. 2. The Review Committee shall consist of twelve members . . . An attempt shall be made to represent the diverse fields of medical practice. The committee may enlist other members to assist in particular cases.

"Par. 3. . . . It [the Committee] shall respond to inquiries according to its judgment. It shall investigate differences of opinion regarding fees for professional services, first on an informal basis and then if necessary by a formal hearing. If an agreement can still not be reached between the aggrieved party, then the Review Committee shall render an opinion as to the usual, customary and reasonable fee for which the patient may fairly be liable, or which the patient's representative may fairly be expected to pay, for the particular medical service in the area where rendered.

"Par. 4. The opinion of the Committee in writing and signed by the Chairman shall be conveyed to each of the parties concerned and shall also be placed on file in the office of the Association. The Secretary shall forward a copy of this opinion to the Board of Censors."

Inclusion of the words "complaints" in Par. 1, and "formal hearing" in Par. 3 point out the difficulties in differentiating Review and Grievance Committees from each other and from Committee on Ethics. By the criteria set by the Health Insurance Council and the AMA, this committee more nearly fits a committee on grievance.

The Hartford County Medical Society: Its Bylaws contain no provision specifying grievance or review committees. A communication<sup>4</sup> explains how and when such a committee is used. "The Review Committee is an Ad Hoc Group under the control of the Board of Directors." In analyzing the action of such a committee where it has functioned, it seems to act as a review committee in giving in-

formation when requested by insurance companies, and as a grievance committee hearing "complaints" about fees.

"... the Review Committee is composed of three representatives from our Medical Ethics and Department Committee as well as three representatives from the Hartford Claims Managers Council. (The Chairman of the Medical Ethics Committee is also the Chairman of the Review Committee.)

"The purpose of the Review Committee is to assess whether or not a complaint emanating from a member company of the Hartford Claims Managers Council or from any responsible source is valid in terms of a breach of ethics, clinical mismanagement, professional misconduct, or excessive fee charges."

### Summary

The Bylaws of the State Society have no provision for either a review or grievance committee. No county in its Bylaws has a grievance committee. Except for Fairfield County, none has a review committee. The functions of grievance and review committees, as outlined and recommended by the AMA, are included under county committees on discipline and ethics. Most counties make no effort

to distinguish review, grievance, and disciplinary committees. The Council acts only as an appeal body in cases of discipline.

Grievance committees handle all sorts of complaints by patients, the lay public and third parties vis-à-vis physicians.

Review committees act only to give information and advice, usually about fees, to patients and third parties, usually insurance companies.

Committees on Ethics or Discipline may handle any complaint or question; theoretically, they should handle only those problems which may infringe on a provision in our Code of Ethics. Most problems, including fees, are not so serious as to be considered unethical or to necessitate disciplinary proceedings with the procedural requirements of a hearing.

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1. Report of the Medical Disciplinary Committee to the Board of Trustees (AMA), 1961.
2. Guides for Medical Society Grievance Committees (AMA).
3. A Report on Medical Society Review Committees in the United States: The Health Insurance Council, 750 Third Ave., N.Y.C.
4. Personal communication, Mr. Joseph L. Gordon, Executive Secretary, Htfd. Cty. Med. Assoc.

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## ON SCIENCE AND CULTURE

In man's history the sciences make changes which cannot be wished away and cannot be undone. Let me give two different examples. There is much talk about getting rid of atomic bombs. I like that talk; but we must not fool ourselves. The world will not be the same, no matter what we do with atomic bombs, because the knowledge of how to make them cannot be exorcised. It is there; and all our arrangements for living in a new age must bear in mind its omnipresent virtual presence, and the fact that one cannot change that. A different example: we can never have again the delusions about the centrality and importance of our physical habitat, now that we know something of where the earth is in the solar system, and know that there are hundreds of billions of suns in our galaxy, and hundreds of billions of galaxies within reach of the great telescopes of the world. We can never again base the dignity of man's life on the special character in space and time of the place where he happens to live.

These are irreversible changes; so it is that the cumulative character gives a paradigm of something which is, in other respects, very much more subject to question: the idea of human progress. One cannot doubt that in the sciences the direction of growth is progress. This is true both of the knowledge of fact, the understanding of nature, and the knowledge of skill, of technology, of learning how to do things. When one applies this to the human situation, and complains that we make great progress in automation and computing and space research but no comparable moral progress, this involves a total misunderstanding of the difference between the two kinds of progress. I do not mean that moral progress is impossible; but it is not, in any sense, automatic. Moral regress, as we have seen in our day, is just as possible. Scientific regress is not compatible with the continued practice of science.—J. ROBERT OPPENHEIMER. "On Science and Culture." *Encounter*, October, 1962, p. 3.



# Subcutaneous Calcification OF The Legs In Chronic Venous Insufficiency

Alfred B. Sundquist, M.D., V. Abraham Kurien, M.D. and Martin Duke, M.D.

■ Subcutaneous calcification and ossification of the legs has been described by Lippmann and Goldin<sup>1</sup> as a frequent late complication of chronic venous insufficiency. On the other hand Grushka and Chagan<sup>2</sup> considered this condition, as opposed to phleboliths, as a rare occurrence.

The following case is of unusual interest due to the massive degree of calcification in the lower extremities of a patient with chronic venous insufficiency, discovered twenty years after treatment for varicose veins with sclerosing injections.

## Case Report

This 74 year old woman, a retired textile weaver, was admitted in December 1964 with a varicose ulcer on the left leg. She claimed that for sometime she had been picking "small hard seeds" out of the ulcer. She had long standing complaints of "jittery legs" and intermittently had been treated for generalized osteoarthritis, tension, anxiety, eczema, and moderate hypertension. She had had several attacks of thrombophlebitis in the left leg resulting in stasis dermatitis of severe degree. Over a period of many years she had received numerous medications including deprol, meprobamate, barbiturates, steroids in small doses, and vitamin B<sub>12</sub>. Twenty years before admission she had received many injections of sclerosing solutions for varicose veins. An X-ray of the left leg taken on March 16, 1944 for an injury was reported "negative for evidence of recent injury to bones or for other osseous pathology."

Physical examination showed a tense, compulsive patient with a blood pressure of 180/100. There was bony thickening about the joints, and a soft systolic murmur was heard at the base of the heart. The superficial veins of the legs were large and extensive, more so on the left than the right side. At the junction of the middle and lower third of the left leg, there was a 1 cm. punched out ulcer. Hard movable nodules measuring approximately four to eight millimeters in size could be felt scattered throughout the subcutaneous tissues of the left leg. The lower portion of the legs showed brawny induration. The left leg measured 13 cm. in its greatest circumference compared to 15 cm. for the right leg. This was considered to be due to a difference in the amount of subcutaneous fat.

X-rays of the feet and legs showed extensive calcification throughout the subcutaneous tissues, with the left leg involved

*From the Medical Service, Manchester Memorial Hospital Manchester, Connecticut, supported in part by a grant from the Gertrude H. Rogers Fund.*

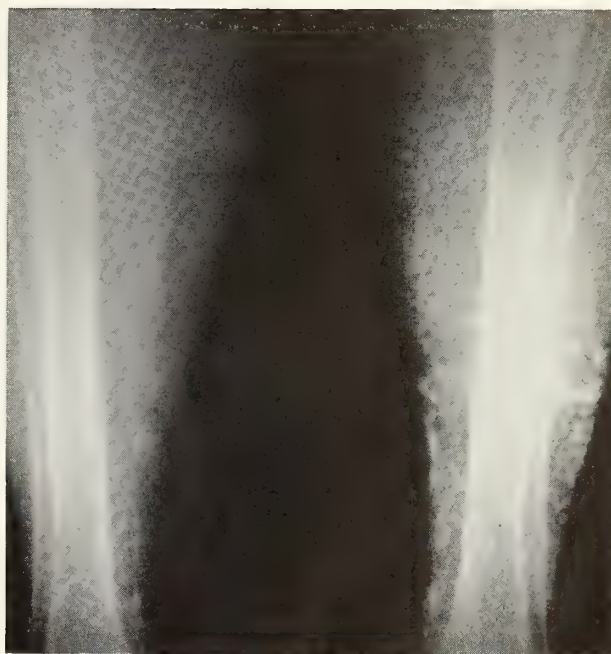


FIGURE I

X-ray of the right and left legs showing extensive subcutaneous calcifications. The left side is involved to a greater degree than the right.

to a greater degree than the right leg (Figure 1). X-rays of the skull, chest, forearms, wrists and hands were negative except for arterial calcification and for extensive hypertrophic arthritis. Laboratory studies showed a serum calcium of 10.0 and 10.2 mg.%, phosphorus of 3.6 and 2.1 mg.%, blood urea nitrogen 28 mg.%, and normal blood sugar and serum protein. Blood count was normal except for a mild eosinophilia on two occasions of 7 and 10%. Urinalysis revealed unexplained hematuria. An intravenous pyelogram showed slight dilatation of both ureters at their midpoint but otherwise was unremarkable. A skin biopsy of the lower extremity revealed nodular areas of calcific material lying free in the subcutaneous tissues and not associated with vascular channels. A chronic inflammatory infiltrate was present in the upper portion of the dermis.

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## Discussion

The absence of metastatic calcification in other tissues, together with the absence of uremia and evidence for parathyroid disease, would suggest that it was the long standing trauma of chronic venous insufficiency that resulted in the calcification seen in this case. The mechanism for this type of deposition of calcium salts in an area of trauma and inflammation, so called dystrophic calcification, is not well understood. One could also speculate in this case as to whether the injections of sclerosing solution was a contributory factor. It is of interest that it was the patient who initially made the diagnosis, or at least prompted further diagnostic procedures, by her description of removing "small hard seeds" from the ulcer. However, such calcification can occur without this history of ulcers or injections, having been reported by Lippmann and Goldin<sup>1</sup> in 10 per cent of 600 middle aged women with chronic venous insufficiency. As pointed out by Bennison and Morales,<sup>3</sup> calcium deposition not only may be a cause for ulcers of the legs, but also may act as a foreign body to prevent healing of these varicose ulcers.

It would appear from a review of the literature that the incidence of calcification of the legs in chronic insufficiency might well be related to the frequency with which X-rays of the extremities are performed. The present case would suggest that in

chronic venous insufficiency of the legs, especially when ulcers and stasis dermatitis are present, X-rays should be performed looking for calcification. Its presence might well be a factor in planning treatment and management.

## Summary

A case of bilateral calcification of the subcutaneous tissues of the lower extremities is presented in a 74 year old woman with long standing venous insufficiency and stasis dermatitis. Of additional interest is the history of prior treatment with sclerosing injections. Though the incidence of this type of calcification is probably more common than reported, being related to the frequency with which X-rays are taken, it would seem that it would be found more often in these patients who develop stasis dermatitis and varicose ulcers.

The authors wish to acknowledge the work done by Dr. Douglas J. Roberts in preparing the photograph of the X-ray.

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## THE HAZARDS OF PROGRESS

The greatest risk that confronts us is not precisely unawareness of new discoveries and the latest findings. No, it is the slow breaking down of the rigour of our scientific method which was devised to ensure bases for our knowledge and to demand proof before admitting the truth of what is new. It is the risk of forgetting Cartesian doubt, that doubt which has been the backbone of our scientific posture. The flood of medical literature not infrequently impedes serene reflection and drowns critical judgment. What we gain in erudition we lose in wisdom.

There are yet other risks. Those prodigies of technique which fill us with enthusiasm and which all too easily deceive us, sometimes cause us to confound the delicacy of the procedure with the rigour of the method. The complicated and wonderful instrument becomes both an aid and a menace. Furthermore there is the heady speed at which we live and the contagion of enthusiasm which finally produces collective illusions and turns us into victims of fashions. Who can doubt that we are suffering these things: It is enough to remember the number of drugs that only yesterday filled the magazines with their flattering results; everybody used them. And today? Who remembers their names?—DR. IGNACIO CHÁVEZ. Speech delivered at the Inaugural Ceremony of the IV World Congress of Cardiology. Universidad Nacional Autónoma de México, México, D.F., 1962, p. 7.



# The Contributions Of The Horse To Knowledge Of The Heart And Circulation

## III. James Mackenzie, Thomas Lewis, And The Nature Of Atrial Fibrillation

H. E. Hoff, M.D., L. A. Geddes, Ph.D., and J. D. McCrady, D.V.M.

### Introduction

■ "Irregularities of the heart are of such frequency, and their presence so readily recognized by both patient and physician, that it is necessary clearly to recognize their meaning and significance. Until a few years ago, their nature was shrouded in obscurity, and in consequence the mystery regarding them oppressed both patient and physician.

"The fact that in some instances irregularity is of serious import has led to the supposition that all irregularities are signs of some grave mischief. In consequence of this, many patients are subjected to unnecessary fears, made to carry out elaborate methods of treatment, and to have imposed upon them burdensome and unnecessary restrictions. . . .

"The advance that has been made in the knowledge of this subject within recent years practically constitutes a revolution. By the combined efforts of clinicians and experimental physiologists, what was recently a complete mystery is now one of the best understood matters in the whole science of medicine. Not only has the scientific aspect been worked out, but by following individual cases for years, and observing how people with irregular hearts have borne the stress of life, a clearer conception has been obtained of the bearing of the different irregularities on the future history of the patients.

"There are three main circumstances which have combined to throw light on irregular action of the heart, viz. the experimental discoveries of the nature of the functions of the heart muscle, the application of graphic records of the jugular pulse to the interpretation of heart irregularities, and the discovery of the remains of the primitive cardiac tube in the mammalian heart and its physiological significance."<sup>1</sup>

So wrote James Mackenzie in 1907, reviewing what was in the main almost wholly his own con-

tribution to medicine. The judgment of history has amply confirmed the validity of his three principal approaches: the experimental study of the physiology of the myocardium, and the adaptation of instruments of precision in clinical investigation, with both viewed against the background of the embryology of the heart and great vessels.

### James Mackenzie And The Analysis Of The Venous Pulse

In 1879 as a somewhat over-age graduate in medicine from Edinburgh, Mackenzie began practice in the Lancashire industrial town of Burnley. By 1907, at the age of 54 he was firmly established in London's Harley Street as the first physician to devote himself exclusively to cardiology, and one of the genuine founders of clinical investigation. The story of his life in those interesting days has often been told.<sup>2</sup> His own words above recount its essentials; his early recognition that some cardiac arrhythmias carry no serious import while others do, and his attempts to analyze the two types by study of the graphic records of radial and jugular pulsations simultaneously registered. This analysis he began as early as 1883, using pneumatic pulse pickups recording on a smoked drum, much after the fashion of Marey's earlier systems. He called

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*Supported by Grant HTS 5125, National Heart Institute, National Institutes of Health, Washington, D. C. From the Department of Physiology, Baylor University College of Medicine, Texas Medical Center, Houston, Texas.*

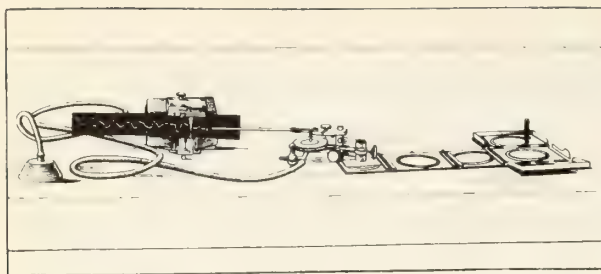


FIGURE I

Mackenzie's single channel pulse recorder. (From reference 3).

this and later direct-inking devices, the Polygraph.<sup>3,4</sup> Figures I and II show two of Mackenzie's devices, after they had been perfected by professional instrument makers.

Because of its meager force and complex form, the jugular pulse recording proved to be much more difficult to record and interpret than the radial pulse, showing in typical records a triphasic complex of waves, as illustrated in Figure III, from one of Mackenzie's earlier papers in which the waves were labelled simply a, b, and c, and were as yet not clearly identified as to origin. The a wave of Figure III—I clearly coincides with the carotid pulse of Figure III—III and later came to be identified as the c wave. The following wave b, is related to the beginning of ventricular diastole and in the future will be known as *v*. It is attributed to the damming up of blood in the auricles and

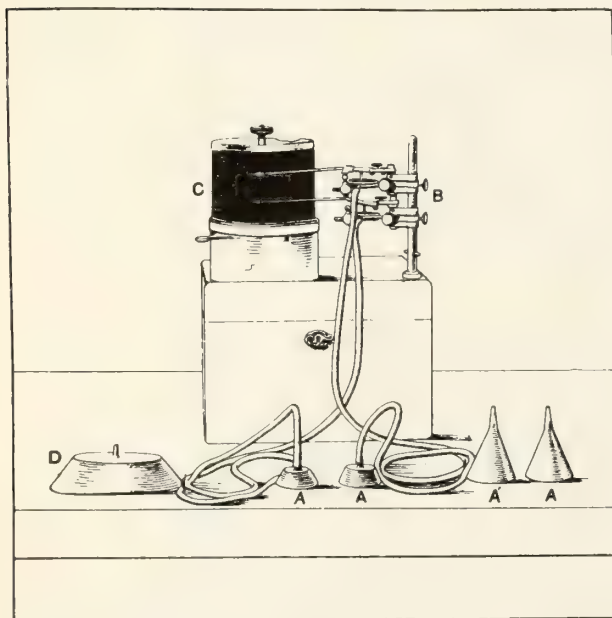


FIGURE II

Mackenzie's two-channel polygraph with tambours for recording and funnels of several sizes for detection of the venous pulse. (From reference 3).

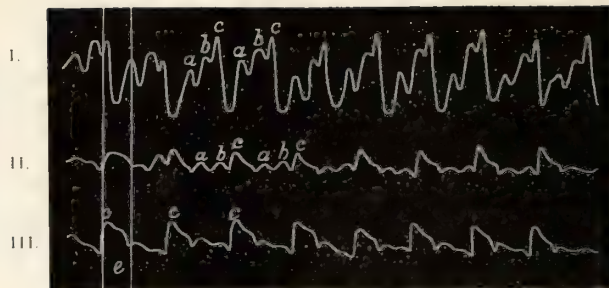


FIGURE III

One of Mackenzie's first published records of the jugular pulse. (From reference 3) It shows the three channel record of the venous pulse (I), venous and carotid pulses together (II), and carotid pulse alone (III). The A-wave of the jugular pulse is identified as coinciding with ventricular systole and the carotid pulse. C and B of the venous pulse are not yet identified as A and V respectively.

great veins during systole and its release into the ventricles as they relax. The wave marked c of Figure III—I will be found to coincide with atrial systole and will be renamed, for that reason, a. In reference to the carotid pulse of Figure III—III the a wave clearly preceded the carotid, or purely arterial pulse, and was assigned to auricular contraction, the c wave was coincident with the arterial pulse and was assigned to a transmitted impulse from the adjacent carotid artery or due to ventricular systole bulging up the A-V septum and valves, while v coincided with the end of ventricular systole and the onset of diastole; it was assigned to the damming back of blood in the auricles and great veins during ventricular systole and the sudden relief of this accumulation as the ventricles relaxed. Figure IV shows how Mackenzie analyzed with simultaneous records of radial and jugular pulse what appears at first to be 2 to 1 block, but is probably total A-V block. Figure V illustrates 3 to 1 A-V block.

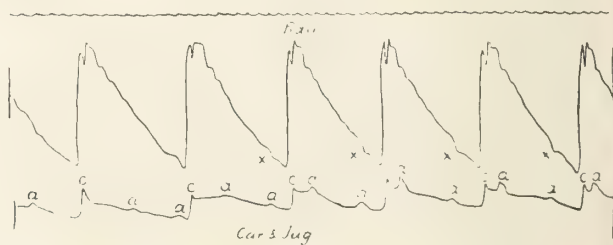


FIGURE IV

Mackenzie's illustration of A-V dissociation. (From reference 7). The auricles are beating regularly at a rate more than twice the ventricles, and the varying A-C interval indicates that this is not a case of 2:1 A-V block, but total A-V block with a coincidental ventricular rate close enough to half the auricular rate to give the appearance at first glance of a 2:1 block.



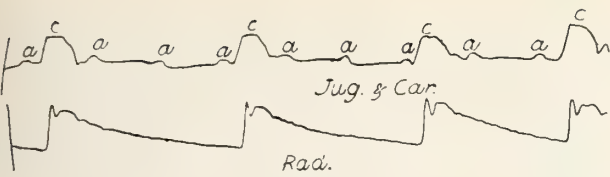


FIGURE V

From the same article as Figure 3, depicting 3:1 A-V block as analyzed by simultaneous registration of jugular pulse (above) and carotid pulse (below). Note that the last *c* wave is preceded by only two *a* waves, and the A-C interval is longer than after the periods with three *a* waves. We now know that this is entirely possible in partial block, as it is usually associated with the Wenckebach phenomenon of progressive increase in P-R interval until a QRS complex drops out. In the next cycle a shorter P-R appears, only to lengthen in subsequent cycles until another impulse is blocked.

It is of course apparent that pulse wave analysis cannot indicate the origin of ventricular systole, as does the configuration of QRS in the electrocardiogram, so that, quite apart from the technical difficulties of the pulse method, of which Mackenzie was an adept, the electrocardiogram was able to offer a greater degree of accuracy in the diagnosis of the arrhythmias than the pulse method. No wonder the British Medical Journal editorialized (1904, p. 650) "A sphygmograph needs as many dexterities as a cricket bat."

The first arrhythmia to succumb to the new tool in Mackenzie's hands was that of the ventricular ectopic beat. Figure VI shows his record of this condition, in which the weak and premature radial pulse marked X coincides with a *c* wave in the venous pulse, followed by an *a* wave, designated at its proper interval by *a'*. Figure VII shows how Mackenzie analyzed the sequence of events to demonstrate how the fundamental rhythm of the pacemaker is not altered in such circumstances, and why, for this reason, the post extrasystolic pause is fully compensatory. In sum, Mackenzie gave an almost complete analysis of such beats, calling attention to 1) their ectopic origin, (which his records could really not demonstrate directly), 2) their prematurity, 3) the compensatory pause, 4) the weakness of the premature beat, 5) the abnormal strength of the following beat, and 6) the tendency for alternation of force following re-establishment of the normal rhythm.

Figure VIII is typical of Mackenzie's care in following his patients, showing two records taken at an interval of 14 years. The first portrays a normal rhythm, the second an example of the irregularity we now recognize as atrial fibrillation. The apex beat is totally irregular in rate and force and there is an all-over increase in the heart rate, while in the jugular pulse there is no sign of a pre-carotid or *a* wave. To Mackenzie this denoted "paralysis" of the auricles, and in one sense this was true; the auricles no longer produced a pre-ventricular con-

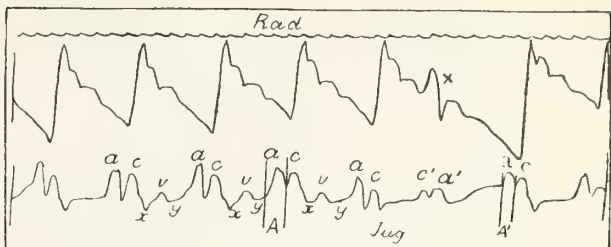


FIGURE VI

Mackenzie's recording (From reference 7) showing the radial and jugular pulses in a case of ventricular extrasystole, the first arrhythmia analyzed by Mackenzie with the polygraph. The *a*, *c*, and *v* waves are repeated in orderly sequence until the beat marked by X in the radial pulse, where a premature *c* wave is followed by an *a'* wave at its normal place in the sequence of atrial beats. The following ventricular pulse follows a pause which "compensates" for the prematurity of the extrasystole, and because of its greater diastolic filling, is more powerful than the other beats.

traction. As Mackenzie was first to point out, as this arrhythmia began in the typical patient with mitral stenosis, the characteristic presystolic murmur ceased.<sup>5</sup>

Along with the atrial paralysis, Mackenzie believed, there occurred a shift of pacemaker to the ventricle, or more particularly, to the A-V node, which for some unknown reason, he postulated, beat irregularly. Noting, however, that many auricles proved to be hypertrophied at autopsy after long-standing atrial fibrillation in man, and that the arrhythmia occasionally reverted to normal, Mackenzie himself raised the question of "what was the auricle doing during this abnormal rhythm? That it was not paralyzed is evident in that it at once returns to work immediately the normal rhythm is resumed."<sup>6</sup> He did indeed consider the possibility that the auricles were fibrillating, but in general he was more inclined to suspect that the impulse generated in the A-V node was transmitted more or less simultaneously to auricles and ventricles, so that the carotid pulse largely obliterated the smaller auricular wave.<sup>7-10</sup>

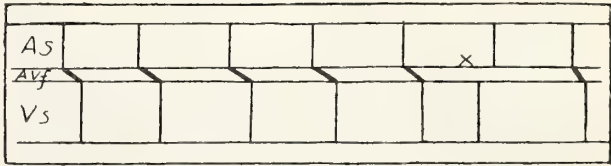


FIGURE VII

Mackenzie's diagram (From reference 7) showing how the ventricular extrasystole in Figure VI does not disturb the fundamental rhythm of the heart, because it is not conducted back to the atria before these chambers have beat spontaneously. For this reason there must of necessity be a "compensatory pause" after the extrasystole.

### Thomas Lewis And Atrial Fibrillation

In 1908 Mackenzie made the acquaintance of a brilliant young Welsh physician, Thomas Lewis. A graduate in Anatomy and Physiology at University College, Cardiff in 1902, and in Medicine at University College, London in 1905, Lewis had been working in the physiological laboratory with Starling, and he was encouraged by Mackenzie to begin a study of the cardiac irregularities. We know now that this study confirmed him as a cardiologist and as a clinical investigator, and indeed as the very prototype of such an investigator. Much later he wrote: "Knowledge requisite to the practice of medicine rests upon a tripod: studies of living men in health and disease; studies of dead men; and correlated studies upon the lower animals. Clinical science in its work embraces all three, but its central and unique province, most fundamental to all work pertaining to the practice of medicine, is that which concerns living men."<sup>11</sup> His contributions to medicine included his classical study on the origin and transmission of the heart beat and on the cardiac arrhythmias, investigations on the response of the small blood vessels of the skin, and a later series on the mechanism of referred pain.

His first major contribution was the elucidation of atrial fibrillation. To this he brought a new tool, the string galvanometer of Einthoven, which was not only sensitive enough to record the small changes in body-surface potentials created by the cardiac action potentials, but rapid enough in its response time to follow faithfully the evolution of these potentials with each beat of the heart.<sup>12</sup>

The first patient to whom Lewis applied this new tool suffered from paroxysmal ventricular tachycardia. From the absence of P waves, Lewis was able to diagnose it as some form of A-V nodal rhythm. The rhythm was however perfectly regular, and afforded no confirmation whatsoever of Mackenzie's postulation of irregularity as a characteristic of nodal rhythms. So stimulated, Lewis obtained records of patients with atrial fibrillation, and noticed the replacement of the P waves by fine oscillations that suggested the presence of fibrillation.<sup>13</sup>

Experiments on dogs showed the same electrocardiographic and polygraphic signs when atrial fibrillation was produced by repetitive stimulation of the atria, and the fibrillatory waves were clearly seen in the exposed heart. Vagal stimulation slowed the ventricular rate, presumably by A-V block, and suggested a similar mechanism for the comparable effect of digitalis in the fibrillating human heart. Mackenzie had earlier made it clear that the main danger in the condition was an excessive heart rate, and that the main effect of digitalis was to slow the rate to some efficient level.

"I now come," wrote Lewis, "to what I regard as the last and most conclusive proof of the theory. The appearance of a fibrillating auricle is quite distinctive. It does not contract co-ordinately—that is to say, as a whole—but its walls stand in diastole, a position of virtual paralysis; yet inspection of the surface shows that its muscle is broken up into a multitude of small areas, each of which seems to be contracting vigorously, but with no relation to the contraction in surrounding areas. When you compare the appearance of co-ordinately contracting and fibrillating auricle, you may draw parallels between this chamber and a surface of water, disturbed on the one hand by great billows and on the other by a downpour of rain. In the normally beating heart the regular waves of contraction give rise to regular beats of the ventricle; in fibrillation haphazard impulses issue from the auricle turmoil and stimulate the ventricle. Thus the irregularity of the ventricular beating is produced. But that is not the point to be emphasized, though it explains the pulse irregularity, on explanation which no other hypothesis attempts. The point to lay stress upon is that the visible signs in the heart are distinctive and easily recognizable.

"You will see from what has been said, how important an actual view of an auricle would be if the heart beat in a grossly irregular fashion. The opportunity came when, in searching for similar disease in the lower animals, I found it in the horse. Largely through the kindness of Dr. Woodruff—whom many of you know, for as a veterinary surgeon he came to study human ailments in this hospital—I was able to show that horses are subject to the same heart disorder, and that the curves given by such hearts are of the same form as those seen in man. The final opportunity of examining a horse suffering from a degenerate heart and giving the recognized signs occurred on Bulford Plain. The chest was opened while the heart was still beating, and I obtained, as did those with me, a clear view of a fibrillating auricle, brought to this state, not by experimental interference, but by disease. It is this observation which has dissolved remaining doubt and which has placed the theory in so secure a position. We now know quite definitely that auricular fibrillation may occur and persist as a manifestation of disease.

"In brief, the original rapidity of the pulse and its irregularity, the character of the irregularity, the loss of the auricular wave in the neck, the loss of the P summit in the electrocardiogram, the loss of presystolic murmurs, the presence of rapid oscillations in the venous curve, the presence of oscillations in the electrocardiogram, the varying rate of the ventricle in a single patient or from patient to patient, the action of digitalis—each and all are clear once the true explanation of the mechanism



is grasped. And this explanation, as I have shown you, is that in such cases we have to deal with fibrillating auricles.”<sup>13</sup>

Within the next year Lewis was able to collect reports on five horses with atrial fibrillation, showing the typical electrocardiographic abnormalities associated with this arrhythmia, and in two of these the fibrillating atria were seen by direct inspection. In none of them was there any evidence of a valvular lesion.<sup>14,15</sup> In 1924 Roos<sup>16</sup> was able to report four more cases of atrial fibrillation in horses. As a general rule, in the horses he studied, the pulse rate was not increased, and might even be slower than usual. The arrhythmia was not associated with valvular disease, and the atrial frequency was close to 450 per minute. Otherwise the electrocardiographic signs were much like those in man and other animals, as shown in Figure IX, taken from his report. Roos found that the arrhythmia was rare in the dog, noting only three cases in his report.

Induction Of Atrial Fibrillation In The Horse

In the studies on atrial fibrillation carried out by the authors, the animals were anesthetized.\* The heart was exposed by appropriate thoractomy and artificial respiration was maintained by means of a piston pump having a maximum stroke-volume of 17 liters. It was a relatively simple procedure to remove the pericardium, to attach recording electrodes to the atrium, and precipitate auricular fibrillation while recording the electrical activity of the atria by the direct leads along with the electrocardiogram from lead II, and carotid blood pressure.

Fibrillation was precipitated by painting a 1 cm<sup>2</sup> area of one atrium, usually the right, with acetyl-beta-methyl choline (5 mg/cc.), a strong parasympathomimetic drug not readily neutralized by the choline esterase mechanism, and then gently scratching the surface of the atrium with a pin. The cholinergic drug greatly shortens the refractory period of the atrial musculature, and makes it possible for the atrium to maintain the rapid firing of its fibers. In the horse a rate of 500-700 per minute is usually recorded, while it is much faster, often as much as 3000 a minute, in the dog. Figure X shows the full spectrum of the electrocardiographic and dynamic changes recorded in the horse: 1) the all-over tachycardia, which as Roos pointed out, is not extreme in the horse, presumably because of an intrinsic inability of the A-V node to transmit rapidly, 2) The total irregularity of the arterial pulse in rhythm and amplitude, 3) the failure of some beats to produce an appreciable



FIGURE VIII

Mackenzie's analysis of atrial fibrillation (Ref. 8). Above is the record of one of his patients taken in 1892, showing what Mackenzie called an "auricular" pulse, that is, one with the usual sequence of a, c, and v waves indicating a normal sequence of chamber contractions.

The lower record is from the same patient in 1907, some weeks after her pulse had become rapid and irregular, but had slowed down somewhat, presumably after administration of digitalis. Now the pulse shows no a wave before the c-v of the ventricular component and Mackenzie termed it a "ventricular" pulse. Although Cushny had reminded Mackenzie of the possibility that this kind of pulse might be the result of atrial fibrillation, Mackenzie in this paper holds to the concept of a "nodal" origin in the A-V region, so that the atrial contribution to the pulse is simultaneous with the ventricular, and hence cannot be identified.

arterial pulse, creating the "pulse deficit" which becomes apparent as the total number of systoles in a given time, as derived from a count of QRS complexes, is compared with the arterial pulse count for the same period, 4) the total irregularity of the QRS complexes in rhythm, and minor variations in amplitude, and 5) the disappearance of the P wave and their replacement with rapid oscillations, which are quite noticeable in this recording from the atrium itself and the right foreleg. The influence of vagal stimulation to slow the ventricular rate, presumably by A-V block, which demonstrates that the ventricular complexes are

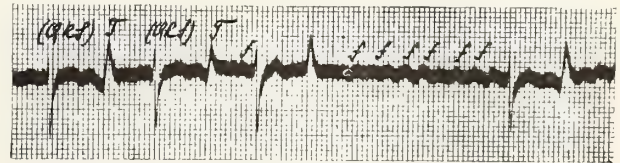


FIGURE IX

Electrocardiogram of atrial fibrillation in the horse, published by Roos (reference 17), showing the typical total irregularity, absence of P waves, and presence of fragmentary f waves.

\* Equithesin, Jensen-Salsberg, Kansas City, Missouri.

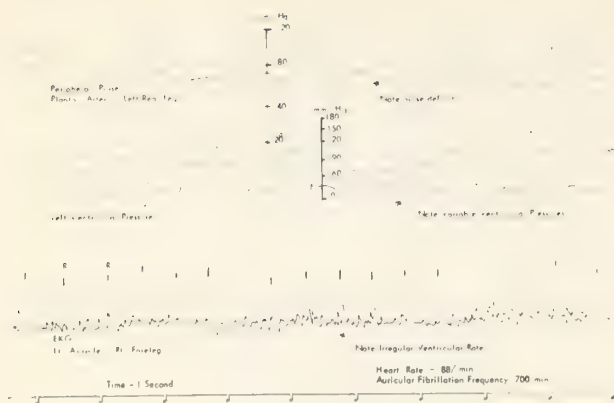


FIGURE X

Atrial fibrillation in the horse, illustrating the classical signs of the arrhythmia in the peripheral pulse, the left ventricle and the electrocardiogram.

evoked by impulses coming, in irregular sequence, across the A-V bridge, and are not the product of impulse formation within the ventricle themselves, is not portrayed in this record.

### Conclusion

Atrial fibrillation is the classical disturbance of the cardiac rhythm in internal medicine. The first great breakthrough in its understanding came when Mackenzie was able by analysis of the jugular pulse to distinguish it from ventricular ectopic beats or extrasystoles, which had no pathological significance, and to diagnose its presence by the absence of signs of atrial contraction in the jugular pulse, from whence his designation of the "ventricle type of venous pulse," and by the complete irregularity of the ventricular beat. He was correct in his interpretation of a failure of auricular systole, not alone from the absence of the *a* wave in the jugular pulse but from the disappearance of the presystolic murmur in patients with mitral stenosis as the arrhythmia began, but neither of his suggestions, either of atrial arrest, or an A-V nodal rhythm with simultaneous contraction of auricles and ventricles, held up under the scrutiny of electrocardiographic analysis at the hands of Thomas Lewis. (It must be recalled that Wenckebach in Leyden independently came to the same conclusions from his own electrocardiographic studies.)

Mackenzie was also correct in ascribing much of the difficulty caused by the arrhythmia to the

tachycardia that normally accompanied it, and correctly employed digitalis to reduce the rate.

Lacking the ability to produce long-standing atrial fibrillation in the usual laboratory animals, Lewis had recourse to the occurrence of the arrhythmia in horses to confirm the presence of fibrillating waves by direct inspection of the exposed heart.

To this day the nature of atrial fibrillation remains in debate, as it also retains its importance as the most frequent arrhythmia encountered in cardiac disease.

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*(This is the third of a series of four articles)*



# THE PRESIDENT'S PAGE

## The Physician's First Consideration--The Health Of His Patient

ONE of the interesting and worthwhile duties of the President of the Connecticut State Medical Society is to attend, when invited, the semi-annual and annual meetings of the county associations which make up the state society. These meetings are always informative and keep the president aware of the problems occurring in each county.

At the Fairfield County Association meeting held last September 29th at the Greenwich Country Club, an excellent attendance of 393 members was present as the meeting started. Among many important items of business a "Resolution on Health Care" was presented by the Public Relations Committee and after some discussion was favorably passed. The Resolution was as follows:

WHEREAS the well-being of the patient is the first consideration of the physician and quality medical care his primary objective; and

WHEREAS all physicians should demonstrate professional concern over the politico-socio-economic forces which are influencing the shape of health care to come; therefore be it

RESOLVED that the Fairfield County Medical Association urges its members and parent organizations to initiate constructive and positive methods of improving and implementing voluntary "third party" and government health care programs, including "medicare"; and be it further

RESOLVED that the Association urges its members to seek wider, more active and influential roles in community, area and state health-related organizations, hospital advisory councils and legislative groups engaged at the grass roots level in shaping the health care of the future.

This writer believes that this resolution is an excellent one and that if taken seriously by physicians offers a positive approach to the medical problems of today. He congratulates the Public Relations Committee of Fairfield County for such a timely and clearly stated resolution. The only way that physicians can tell the story of medical care needs is to be active with other interested citizens and work together on all phases of community development which involve the health of the people.

At the special A.M.A. House of Delegates meeting on October 2-3, 1965, the House urged "every physician, regardless of the extent of his involvement, to render whatever advice and assistance he can so that regulatory changes and/or legislative modifications may be suggested or sponsored by the American Medical Association in order that the best interests of the public and the profession may be protected in the provision of medical care."

Obviously all physicians at national, state or county levels, who are aware of the health problems of today, are asking their colleagues everywhere to cooperate with everyone concerned in providing the best health care for all those who need it. The necessity for such combined efforts by all providers of medical services has never been so urgently presented before. The Connecticut State Medical Society wants every member to study these problems and contribute his advice and efforts in the days ahead.

JAMES R. CULLEN, M.D.

## A SPECIAL REPORT OF THE CSMS COMMITTEE ON HOSPITALS

### Subject: Utilization Review Committees Under Part A Of P.L. 89-97 (Medicare)

*The establishment, composition and function of utilization review committees, as called for in the new Medicare Law, are engendering a good deal of interest—and even some controversy—at both national and local levels. On November 17, the Council approved the following special report on this subject, prepared by the Committee on Hospitals, and directed that copies be sent to Commissioner Foote and the chiefs of staff and administrators of our community hospitals, and that the report be published in the Journal for the information of the members of the Society.)*

On October 13, 1965, at a well-attended meeting, the CSMS Committee on Hospitals was joined by Franklin M. Foote, M.D., State Commissioner of Health, to discuss certain matters relating to the implementation in Connecticut of the provisions of Part A (Hospital Insurance Benefits for the Aged) of the new Medicare Law, P.L. 89-97. By direction of Governor Dempsey, and under the supervision of the Commissioner, an agency is to be set up within the Health Department to evaluate and certify hospitals, nursing homes, and related facilities as to their qualifications to participate in the programs provided for by Part A.

The meeting was arranged at the request of Dr. Foote, and the Committee is most appreciative of his willingness and desire to receive the opinions of the medical profession to guide him in taking a sound approach to this obviously monumental task. Several of the more complex aspects of the certification program were examined briefly, but the bulk of the discussion was devoted to the composition, duties and *modus operandi* of the "utilization review committee" which the Medicare Law makes an integral requirement for the certification of facilities which desire to participate under Part A.

Following this lengthy exchange of ideas with the Commissioner, and having had opportunity to review copies of P.L. 89-97 and additional materials obtained from the AMA and other professional sources, the Committee held a special meeting on November 10 for the express purpose of developing a set of recommended "statements of policy" for the establishment and operation of Medicare utilization review committees in Connecticut. The recommendations follow:

(1) The Committee on Hospitals has recommended previously (1962) that, *as a function of the medical staff*, each community hospital in Connecticut should establish and operate a utilization review committee for the following purposes: (a) to promote optimum utilization of hospital services by members of the staff, and (b) to stimulate the

interest of physicians in the multiple factors which contribute to the *cost* of furnishing hospital services and, hence, to the *price* of such services to the consuming public. Since 1962, substantial voluntary progress has been made toward implementing this recommendation by member institutions of the Connecticut Hospital Association, and it is understood that the Joint Commission on Accreditation of Hospitals will probably include a functioning URC as a requirement for full accreditation in the future.

(2) The Committee on Hospitals believes that, in keeping with the principal objectives of hospital tissue committees, surgical audit committees, and others, the primary goal of *any* hospital utilization review committee should be to promote the best medical interests of *all* patients. For this reason, the Committee is of the opinion that the operation of a URC under Part A of the Medicare Law is the proper responsibility of physicians.

(3) The Committee on Hospitals recommends that hospital Medicare utilization review committees be composed of physicians selected from active members of the medical staffs of the institutions concerned, such appointments to be made for each institution by the active members of its staff, or, if authorized by the active members, by the president of the staff.

(4) The Committee on Hospitals recommends that each institution make available to its Medicare utilization review committee the services of representatives of the hospital administration, the social service department, the tissue committee, the surgical audit committee, and such other resource personnel as may be found necessary to enable the URC to carry out its assigned duties. In addition, the administration should make available to the URC such secretarial and related help as may be needed to accomplish its required paperwork (forms, reports, etc.), such help to be furnished at the expense of the institution as a compensable cost of hospital care under Part A of P.L. 89-97.



(5) The Committee on Hospitals foresees the strong possibility that members of a Medicare utilization review committee will be called upon to devote substantial amounts of their time to service with the committee. The Committee on Hospitals therefore recommends that active members of the medical staff making such sacrifices of their professional and/or personal time be suitably reimbursed for same by the hospital administration, such reimbursement to be charged to the government or appropriate fiscal intermediary as a compensable cost of hospital care under Part A of P.L. 89-97.

(6) The Committee on Hospitals is convinced that the physician members of a Medicare hospital utilization review committee, in the performance of their duties, may be required to assume "professional liability" above and beyond that which is normally covered by individual malpractice insurance policies. For this reason, the Committee on Hospitals recommends that hospital administration and/or the Secretary of Health, Education and Welfare arrange to guarantee immunity against such liability to the members of a URC in matters directly related to the performance of their assigned duties.

(7) The Committee on Hospitals finds that the establishment and operation of a Medicare utilization review committee to cover extended-care facilities and home-care agencies may present certain different problems under certain circumstances. If these facilities are fortunate enough to have large, self-contained medical staffs, the Committee on Hospitals recommends that such facilities form their own Medicare utilization review committees in keeping with recommendations 1 through 6. In cases where a community hospital has acquired a number of satellite extended-care facilities, with working transfer and administrative agreements, the Committee recommends that the hospital Medicare URC also review utilization of services in the satellite institutions, it being understood that the increased work load would call for increased reimbursement to the members serving in such a capacity.

When neither of these methods is possible and/or practical, the Committee on Hospitals recommends that an appropriate county or local medical society be asked to appoint a Medicare utilization review committee, composed of members of that society, to service one or more facilities in its geographical area which are in need of same. In such instances, it is recommended that the same conditions for reimbursement and protection against professional liability be arranged for physicians serving on Medicare URC's as are described in the previous recommendations.

(8) The Committee on Hospitals recommends that the Council approve (for CSMS) the foregoing statements of policy regarding the establishment and operation of utilization review committees under Part A of the Medicare Law and make them available, as information, to all parties having a legitimate interest in these matters, and, in particular, to the Commissioner of Health, Dr. Foote.

Respectfully submitted,  
LEOPOLD M. TRIFARI, M.D., Chairman  
CSMS Committee on Hospitals

### How To Justify Treatment Risk

For an objective evaluation of drug toxicity, emphasis should be placed on the relative usefulness of a given drug as well as on its potential harmfulness. Even such benign and essential agents as oxygen or water may be harmful when used in-advicely as therapeutic agents. . . . Drugs of such established value as digitalis are potentially lethal when used in excess. It is thus apparent that the potential toxicity of drugs must be counterbalanced by emphasis on their proper usage. The physician should be ever cognizant of the potential dangers of his medications as well as of their efficacy, and balance the two in determining the desirability of taking the risk involved. He should not use amidopyrine to treat a headache, but should have no hesitation in risking its potential harm when he needs an antipyretic for a patient with leukemia. The glucocorticoids should not be used in most patients with rheumatoid arthritis, but should never be withheld from patients with pemphigus.—Arthur Grollman, M.D., in *Texas State Journal of Medicine*, 61: 1, (Jan.) 1965.

### PROFESSIONAL OFFICE SPACE TO LEASE

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## SUMMARY OF PROCEEDINGS

### HOUSE OF DELEGATES — SEMI-ANNUAL MEETING

New Haven, Connecticut — December 9, 1965

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#### Reports, Addresses And Remarks

Reports were presented by:

The Secretary: Waldo E. Martin, Milford.

The Council: Stevens J. Martin, Hartford, Chairman.

AMA Delegates: Norman H. Gardner, East Hampton, Max Caplan, Meriden, and Ellwood C. Weise, Sr., Bridgeport.

Remarks were made by:

The President: James R. Cullen, Hartford.

The President-Elect: Orvan W. Hess, New Haven

The Vice-President: E. Tremain Bradley, Norwalk.

The Speaker of the House: Kenneth F. Brandon, Hartford.

The Commissioner of Health: Franklin M. Foote, Hartford.

Chairman of the COMPAC Board of Directors: Francis Gallo, Winsted.

The General Manager: William R. Richards, New Haven.

The presentations, if submitted in writing, will be published in *CONNECTICUT MEDICINE*.

#### The Budget For 1966

Recommended by the Council, it was VOTED to approve the 1966 Budget as presented, and to set CSMS membership dues for 1966 at \$50.

#### COMPAC Billing

Recommended by the Council, it was VOTED to adopt a motion as follows:

IT IS MOVED: That the House of Delegates approve the inclusion of Connecticut Medical Political Action Committee membership dues, as a voluntary (non-tax deductible) item on the same statement with the annual membership dues of the Connecticut State Medical Society and the County Medical Associations.

#### Authorizations To Form CSMS Sections

Recommended by the Council, it was VOTED to authorize stipulated groups of members of the Society to form sections as follows:

A Section on Pediatrics

A Section on General Practice.

#### Confirmation Of Interim Appointments

It was VOTED to confirm several interim changes in the membership of Committees elected by the

House, which have been approved by the Council. To fill the office of Vice-Speaker of the House of Delegates, created by the resignation of Jachin B. Davis, New Haven, it was VOTED to confirm the appointment by the Council of Henry Caplan, Meriden, to replace Dr. Davis as Vice-Speaker for the balance of his current term (until April 26, 1966).

#### Resolution From The New Haven County Medical Association

It was VOTED to adopt a resolution introduced by the NHCMA as follows:

BE IT RESOLVED: That the House of Delegates of the Connecticut State Medical Society direct the Council to undertake the accomplishment of the following objectives:

(1) Institution of payment for heretofore unpaid services of physicians to local and state in-hospital and outpatient welfare recipients.

(2) Provisions for fee-for-service attendance at privately operated clinics and other medical care facilities.

and be it further

RESOLVED: That in all negotiations in these matters, the Council should utilize the formulas provided by the Relative Value Schedule adopted by the CSMS House of Delegates in April, 1965, and be it further

RESOLVED: That the accomplishments of the Council in these matters be reported to the House of Delegates at its next meeting.

#### Resolutions On Separate Billing Of Hospital Patients

It was VOTED to adopt two identical resolutions- introduced respectively by the CSMS Section on Radiology and the CSMS Section on Pathology, as follows:

WHEREAS: The Section (on Radiology and on Pathology) of the Connecticut State Medical Society has adopted the principle that all hospital patients be billed separately for the professional services of doctors of medicine, and

WHEREAS: This principle is in accordance with the positions adopted by the American Medical Association and the American College of Radiology (and the Council of CSMS—see below) therefore be it



**RESOLVED:** That the House of Delegates of the Connecticut State Medical Society support the principle that all hospital patients be billed separately for the professional services of doctors of medicine, and notify the Connecticut Insurance Commissioner, the Connecticut Compensation Commissioner, the Connecticut Hospital Association, and all recognized third party payors of this action.

In a related action, it was **VOTED** to adopt a recommendation of the Council as follows:

**RESOLVED:** That the House of Delegates of the Connecticut State Medical Society, at its semi-annual meeting on December 9, 1965, support the principle of separate billing for the professional services of practitioners of the (so-called) hospital based specialties.

### **On The 1965 Kerr-Mills (MAA) Amendments**

Having heard in the Report of the Council that efforts have been made to rectify the "legislative oversight" which occurred in the 1965 General Assembly's action to amend the Kerr-Mills Statutes, and being apprised that a special session of the Assembly had been called by the Governor for Monday, December 13, 1965, the following motion was adopted:

**IT IS MOVED:** That the House of Delegates ask the President (Dr. Cullen) and the Chairman of the Council (Dr. S. Martin), in consultation with Mr. Joseph Cooney (CSMS legislative agent), to petition Governor Dempsey and/or a member of the General Assembly to add to the agenda of the special session of the General Assembly called for Monday, December 13, 1965, an item to change the MAA Amendments of 1965 so as to truly reflect the original intent of the MAA statutes to cover in-hospital care of MAA beneficiaries by physicians of their own choice.

*N.B.*—Drs. Cullen and Martin were subsequently advised by legislative counsel that it would not be possible to carry out the wishes of the House of Delegates because "the decision of the leaders that this short one-day session (on Monday, December 13) should be limited to (correcting emergency situations in Waterbury and East Haven), even to the exclusion of other meritorious matters."

### **On Reports At Semi-Annual Meetings**

**IT IS MOVED:** That, in the future, all reports of officers, delegates and committees made to the Semi-Annual Meetings of the House of Delegates be published, to the extent possible, in the Delegate's Handbook with the call to the meeting, as they are for the Annual Meetings.

## **REPORT OF THE COUNCIL**

MR. SPEAKER, MR. PRESIDENT, MEMBERS OF THE HOUSE OF DELEGATES AND DISTINGUISHED GUESTS:

Progress is a function of time as well as of effort. James Bryant Conant once said: "Behold the turtle! He makes progress only when he sticks his neck out." It seems to me that nothing could be more axiomatic and appropriate than *that* for the medical profession today, particularly for those among us who are inclined to be lethargic, complacent, credulous and indifferent. This is the time for us to stick our necks out—to move and be heard. Perhaps the enactment of the Medicare Law was the stimulus we needed.

At the five sessions of the Councils which have been held since the last meeting of this House in April, your state officers and county representatives have devoted a great deal of time and effort to studying and attempting to resolve wisely a seemingly endless number of important questions that have presented themselves—month after month. Since each of you has received copies of the detailed minutes of our meetings, I propose to summarize only certain selected items which I believe will be of special interest to you today.

### **1. Organization For 1965-66**

At its May meeting, the Council elected your reporter as Chairman for a third consecutive term—an honor and an opportunity for service which I greatly appreciate. At the same meeting, the subcommittees and other special committees of the Council were appointed for the ensuing year. The work of these groups—and the work of the many Standing Committees and Special Committees elected by the House—is to conduct studies of assigned problems, to gather information, and to make reports with recommendations to the Council on a wide variety of subjects. We can all be proud of the way they do their jobs, and we are grateful to them for their worthy contributions to the benefit of the public as well as the profession.

### **2. The LCMA Bicentennial Celebration—1966**

Of special historic interest to us all is the forthcoming 200th anniversary of the Litchfield Association—which points with understandable pride to the fact that it is the oldest county medical association in the country, except for a few which have since gone out of business. The Celebration will be held during the month of June next year, and the Council has appointed an Ad Hoc Committee to work with the county people who are planning the event. The Society is committed to participate in this worthy undertaking, and will assist in all ways possible to make the program a successful one.

### **3. Corporate Gift To COMPAC**

Pursuant to the April directive from the House of Delegates, the Council voted to donate the sum of \$5,000 to the Connecticut Medical Political Action Committee. As in 1964, when COMPAC was given \$3,000, it is understood that the COMPAC Directors will use this money exclusively for political *education* purposes.

While both these donations were given prior blessing by our legal counsel, they have produced two internal side-effects which I think should be brought to your attention. The first of these will be brought up when the Budget for 1966 is presented later in this meeting, but—in brief—it is that the gift of \$5,000 to COMPAC made it necessary for us to tap our general reserve fund again, a practice we have

had to follow rather often in recent years because of being faced with major expenditures which were unbudgeted for those years. I mention this here for the reason that if it is the intention of the House to make an annual donation to COMPAC, I feel it ought to be included as an identifiable item in our future budgeting.

The second side-effect—which, unfortunately, also concerns our finances—was that, in looking into the legality of our making a donation to COMPAC in 1964, our attorney was forced to stir up the previously untroubled waters of our tax-exempt status with the Internal Revenue Service. We have always understood our IRS classification to be 501 C (3)—meaning “scientific and educational”—which made it *not* necessary for us to pay state and federal taxes for unemployment insurance. In the course of Mr. Nickerson's study, however, the Internal Revenue Service ruled that we were operating under 501 C (6)—called “business league”—and had been since our employees were placed under Social Security in 1951. As a consequence, we must now discharge our responsibility to pay back-taxes for unemployment insurance and, while the total liability is still being negotiated by legal counsel, I can assure you that it is likely to come to a good deal more than just pennies-a-day.

#### 4. The Relative Value Schedule

As directed by the House in April, the Council purchased 4500 copies of the 1964 Edition of the California Relative Value Studies, and distributed one to each member of the Society. The document was accompanied by a printed informational letter concerning usage of the Schedule and also listed the minor changes in the Section on Medicine that the House approved. Upon his election, it is planned to provide each new member of the Society with a copy and, at the request of the component associations, to mail one to any physician who is considered to be a *bona fide* applicant for county membership. By so doing, it is hoped that all present members and even prospective members of the Society will become familiar with the Relative Value Schedule and be prepared to note such unit changes and additional usages as may be authorized by the House, from time to time.

The purchase, printing and distribution costs of this project will amount to about \$5,000 and, in passing, may I clear up a little misunderstanding which appears to exist in some quarters. During the past several years, I have heard it said—mostly in criticism—that the Relative Value Study cost the Society “\$35,000” or “\$50,000” or even more. The fact is that *both* the Opinion Survey and the Relative Value Study (except for the mailing I have just referred to) were completed within the budget of \$30,000 originally authorized by the House of Delegates in 1959. I do not have the exact figures at hand, but about one-half of the total—or about \$15,000—was spent for each of these two studies, and any additional expenditures for either have been, or will be, presented to the House for approval.

#### 5. Hospital Planning Commission

As has been reported to the House previously, the Connecticut Hospital Association has had under consideration for several years the possibility of establishing a hospital planning commission for Connecticut which would operate on a statewide basis. At the CHA's annual meeting last June, formal action was taken to authorize the Association's Board of Trustees to draw up plans for such a Commission, which, after being launched by CHA, would become a more

or less autonomous body. Several months ago, a Steering Committee appointed by the Board presented a plan to the Association's semi-annual meeting which was enthusiastically accepted and is now in the process of being implemented.

CHA will establish a “Hospital and Related Facilities Survey and Planning Commission” for the purposes of: “Measuring future needs for hospital and health care in Connecticut”; “Creating over-all plans for the efficient and economical development of a hospital and health care system that will most adequately meet our state's needs”; “Measure financial requirements for providing adequate health and hospital care facilities in relation to estimated resources available”; “Helping to coordinate hospital services within Connecticut and, in some cases, with other states bordering service areas”; “Promoting joint interests of hospitals, the medical profession, and other interests on a statewide basis”; and “Informing the public of the financial needs of hospitals and increasing public knowledge and understanding of hospital and other related health services in the state.”

The Society has been invited to nominate qualified physicians for appointment to membership on the Commission who, as initial appointees, will be approved by the CHA's Board of Trustees. The total membership of the Commission may be as many as thirty, with approximately one-half of this number being people who are not associated directly with hospitals, providers of services, or payers of services. Having been apprised on several occasions in the last year or two of the Society's interest in participating in any hospital planning activities to be conducted on a statewide basis, the CHA Board recently invited the Society to participate in its project and to make nominations—for Commission membership—of qualified physicians to represent medical practice. The Council found the conditions surrounding the initial invitation to be somewhat “disappointing” (i.e., sixteen nominees were to be offered, of which only four would be selected; a request that each name be accompanied by a “pedigree” of qualifications, etc.). Through the medium of a joint Ad Hoc Committee meeting, and at the suggestion of the Council's representatives, the CHA Steering Committee agreed to accept six physician-nominees to represent medical practice who are “civic-minded, highly respected and knowledgeable,” and that up to 10 or 12 nominations could be made, if desired.

A large majority of Council members found these new terms to be a good deal more acceptable, and it was voted to direct the President, the Chairman of the Council and the Chairman of the Committee on Hospitals to select the six members of the Society to be nominated. In the near future, these selections will be made and presented to the CHA Board.

As many of you know, the AMA has advised—and even urged—state and local medical societies to participate actively in hospital planning programs, wherever they are in operation. This does not mean that there is overwhelming enthusiasm for hospital planning on the part of most practitioners; it means only that hospital planning is here to stay and that physicians can either elect to sit in, with the hope of having their views reasonably accommodated, or they can remain aloof—disclaiming all responsibility for the results—and read about what has been decided by others. I think it is fair to say that a majority of Council members favor the first alternative—even if it may prove ultimately to be only the lesser of two evils.



## 6. The Journal

For several years now, the House has been apprised that *Connecticut Medicine* continues to operate at a deficit—a deficit which has increased from only 4 or 5 thousand dollars in 1959 to approximately \$20,000 in 1964. The latter figure is expected to obtain in 1965 and, probably, in the foreseeable future. The anticipated revival of lavish pharmaceutical advertising in state journals has failed to occur, despite the fact that the Kefauver drug hearings have long since disappeared from the front pages of our newspapers.

In February we conducted a "readership survey" for the Journal, the raw results of which reported at the April meeting. An Ad Hoc Committee, chaired by Dr. Orvan W. Hess of New Haven, studied the information obtained by the survey and reported its findings and recommendations to the Council as follows:

(a) The "Readership Survey" did not warrant a conclusion that the Journal should be discontinued as the principal publication of the Society, or that its present scientific format should be modified appreciably.

(b) The question, therefore, is not *whether* the Society should continue to publish the Journal but whether it can *afford* to do so in the light of present excess of expense over income (nearly \$20,000 in 1964).

(c) The following measures should be carried out to place the operation of the Journal on a more nearly self-sustaining financial basis:

- (1) Economize in production costs
- (2) Seek additional sources of revenue
- (3) Re-evaluate the entire Journal's financial picture before preparing the 1967 Budget

The Committee's report was accepted, and every effort is being made to carry out its recommendations. We are hopeful that the Journal can be continued in its present form, but, if the deficit cannot be reduced to a reasonable level, the House will have to decide the question of whether the Society "can afford" to underwrite the operation on a losing basis indefinitely.

## 7. Medical-Economic Activities

(a) *The Committee on Third Party Payments:* When the House adopted the Relative Value Schedule last April, it adopted a recommendation that the various sections and groups be asked to suggest conversion factors to be applied to the Schedule when used by authorized committees to try to negotiate realistic payment schedules with government agencies—and *only* with government agencies. Dr. Howard Ente and his Committee on Third Party Payments have been directing their energies to completing this difficult assignment. We are told that they have encountered a few snags which, in the long run, may be turned to good use. Several of the sections report that, in their judgment, certain listed medical services need revision of the unit values and Dr. Ente has recommended that the Committee on Relative Value Study be reactivated by the Council to study these proposed revisions and make appropriate recommendations to the House. Also, his Committee has asked for authorization to explore cost-accounting in relationship to the furnishing of medical services by private practitioners so as to be able to use sample cost analyses as an additional bargaining feature with government agencies when negotiating payment for doctor-care—much as hospitals, nursing homes and others have been doing for quite some time.

In the light of Medicare's enactment, both as to Title XVIII (health benefits for the elderly) and Title XIX (the expanded programs of public assistance), it is clear that the profession will need as many of the modern tools of medical economics as it can muster to avoid government dictation, and we believe that our Third Party Payments Committee is taking constructive steps toward developing some for us.

(b) *The 1965-66 Dependents' Medicare Agreement:* Although the Advisory Committee on Medicare Plan did not recommend any changes to be sought in the Dependents' Medicare Agreement for the coming year, the Council expressed doubt that it should be renewed without being subjected to a thorough study to determine if it reflected the principle of parity of payments to physicians, in line with usual and customary fees—a CSMS policy adopted last Spring. It is interesting to note that this action is in accord with the New Haven Association's resolution which you have on your agenda today.

A six-months extension of the present Agreement has been granted by ODMC in order to prevent interruption of benefits paid on behalf of eligible military dependents, and, meanwhile, the Medicare Advisory Committee and the Third Party Payments Committee have been asked to review the payment schedule in the light of our present policy and to report their findings to the Council.

(c) *The 1965 Kerr-Mills Amendments:* As you all know by now, the 1965 General Assembly passed an amendment to the Medical Assistance for the Aged statutes which, by interpretation of the Attorney General's office, caused Welfare Commissioner Shapiro to discontinue payment for in-hospital services rendered by physicians to MAA beneficiaries, on and after October 1. If you have read the comprehensive report on this development that was published in the November issue of our newsletter, *Connecticut M.D.*, you will have learned that practically everyone from Governor Dempsey on down agrees that the amendment—as written and as interpreted by the Attorney General—constitutes a "legislative oversight" which was entirely "unintentional." Thus far, however, it appears that no one has the authority to undo the wrong without further action by the General Assembly—which is not scheduled to meet again until 1967.

The Council has taken the position that the amount of money involved (less than \$200,000 a year) is not the important issue in this matter. Rather, it is our position that the interruption of patient care and the taking away of free choice of physician from some 20,000 elderly people is the principle which we desire to defend. Governor Dempsey has recognized the validity of our point of view and has taken a personal part in attempting to correct the error. He arranged a meeting between the Commissioners of Health, of Welfare, and of Finance and Control and representatives of the Society to review the situation, and, on December 6, Dr. Richards, Dr. Friedberg (Chairman of our Committee on State Legislation) and your reporter met with the Commissioners and their aides at the Capitol Building. After an hour and a half of highly exhilarating exchange, your representatives came away with the feeling that they had received a great deal of information but not much of any satisfaction—at least, not as far as the basic issue was concerned. In brief, we were given to understand that some sinister Mr. X—identity unknown—must have sneaked in under dark of night and tricked the General Assembly into passing the amendment; that the Attorney General's hands were

tioned—he couldn't have interpreted the amendment in any other way; and that, as matters now stand, nothing—not even an executive order of the Governor—can right this unintentional wrong. We intend to pursue the matter further but, at the moment, the outlook for a meaningful settlement is not bright.

To help cheer up your rather depressed representatives, however, Commissioner Shapiro—with nodding assent from Commissioner Conkling—let us in on his plans for next year, when the Medicare Law goes into effect. The Welfare Department is sending out letters to all persons entitled to either OAA or MAA benefits, urging them to enroll in the Part B program which will cover physicians' services and other services not covered under Part A, that is available to all people over 65. For those receiving Social Security cash benefits (about 14,000) the Department will reimburse them for the \$3 a month deducted from their Social Security checks. For those not eligible for cash benefits (about 6,000), the Department will pay their \$3 enrollment fee directly to HEW. In addition, the Department will be responsible for covering for both groups the \$50 deductible and the 20 per cent co insurance obligation which are called for under Part B policies.

When Medicare's Title XIX goes into effect in July, placing all public assistance medical programs under one umbrella, the Commissioner plans also to make *direct* payments for comprehensive care (*including* in-hospital care by physicians) for dependent children, the blind, the disabled and all others entitled to tax-supported help. This, he estimates, can be done at a cost of about \$645,000 a year for in-hospital doctor-care *alone*, using a payment schedule of 75 per cent of the CMS Preferred Contract (which obtained under MAA, prior to the 1965 amendment).

By these proposed measures, the Commissioner hopes to go far beyond merely making up for the temporary injustice of current MAA policy. If implemented fully, his new plan could practically eliminate ward service in community hospitals for the reason that everyone receiving tax-supported medical care would then be entitled to receive in-hospital care from the physician of his choice and have a mechanism for payment for same.

In all fairness, we think the Commissioners are to be commended for contemplating such a program. However, as a word of caution—which your representatives expressed at the meeting—it remains to be seen what kind of a payment schedule the Part B contracts will offer to physicians, and, in any event, how much longer practitioners will stand for fixed, substandard reimbursement for their services when governmental agencies claim to be assuming responsibility for (and I quote) “paying the doctor's bill.” Politicians promise all these good things to the people, bureaucrats then try to avoid public criticism by clamping down hard on expenditures and, for some strange reason, the providers of medical services are expected to make the politicians and bureaucrats look good by accepting token payments because the patients are classified by them as indigent. This unwarranted exploitation of our time-honored tradition that no one should fail to receive medical care, regardless of ability to pay, is entirely contrary to the Society's policy regarding parity of payments to physicians when government elects to foot the bill. It will be an uphill struggle to put our policy into practice, but—with the enactment of Medicare—we believe that most of our members are beginning to see the light

and will want their representatives to fight the good fight on their behalf.

## 8. Medicare

Medicare, of course, is now the law-of-the-land, having been enacted by the 89th Congress and signed by President Johnson in July of this year. For the first time in its history, the AMA House of Delegates met four times in a period of twelve months—holding two Special Conventions as well as the two regularly scheduled sessions. It goes without saying that the June, October and November meetings dealt almost exclusively with Medicare and the Heart Disease, Cancer and Stroke legislation, and their potential impacts on the private practice of medicine. I know our AMA Delegates—Dr. Weise, Dr. Max Caplan, and Dr. Gardner will report to you today on the proceedings and conclusions of those important assemblies, so I will limit the Council's report on these matters to what has been going on in Connecticut during the past five months.

(a) *P.L. 89-97—Part A*: I am sure most physicians will share with me a feeling of great satisfaction that Governor Dempsey has wisely designated Commissioner Franklin M. Foote and the State Health Department to be the state agency to undertake the monumental task of certifying our hospitals, extended-care facilities and home care agencies for participation in Part A of Medicare—the hospital insurance benefits program. In addition to accrediting the premises and personnel of these providers of services, the Commissioner will also have considerable jurisdiction over such related matters as Medicare utilization review committees, drug formularies, and so on. The Council has expressed appreciation to Dr. Foote for his voluntary decision to establish close liaison with the Society, through several of its key committees, for the purpose of obtaining professional advice to assist him in establishing sound and workable certifying criteria in the latter areas. I believe he plans to be present at this meeting of the House, and I hope he will give you some of his own views on how he plans to carry out such a major assignment.

(b) *Part A—Recommended Criteria For Medicare Utilization Review Committees*

After consulting at length with Commissioner Foote, studying the Medicare Law itself, and reviewing literature on the subject from national and local professional sources, the Committee on Hospitals filed a special report with the Council which contained a series of policy statements on the admittedly controversial subject of Medicare utilization review committees. The Council approved the report and its recommendations, and you have all received an informational copy of it in the back of your Delegate's Handbook. The report has been sent to Dr. Foote, to the chiefs of staff and administrators of all community hospitals, and will be published in an early issue of *Connecticut Medicine* for the information of our members.

(c) *Part A—the Committee on Aging*

At the November meeting, the Council was joined by Drs. Pelz and Friedberg of the Committee on Aging, who informed us that, in their opinion, the enactment of Medicare and its implementation next July and thereafter will certainly magnify the problems which already exist in extended-care facilities, such as nursing homes. After exchanging pertinent ideas and information with Drs. Pelz and Friedberg, the Council voted to endorse, in principle,



series of objectives which the Committee on Aging feels must be achieved. In general, they call for the Society to take leadership in developing programs which will raise the standards of care in nursing homes, increase the supply of trained personnel who can serve the elderly effectively and with understanding, and assist in establishing approved mechanisms for reviewing utilization of such facilities by Medicare patients. In addition, the Committee was authorized to establish formal liaison with representatives of extended-care facilities in Connecticut, and to take steps and make recommendations to the Council which will lead to the attainment of the objectives just described.

(d) *Part B—Fiscal Intermediary for the Voluntary Supplementary Insurance Program*

The Council has neither volunteered, nor been requested, to express a preference for any insurance carrier or prepayment agency to be designated by the Secretary of Health, Education and Welfare as "fiscal intermediary" for the Part B program in Connecticut. However, from unofficial sources, the Council has been apprised that several companies—including Connecticut Medical Service, Inc.—have applied to the Secretary for such designation. In considering a letter addressed to our esteemed President, Dr. James R. Cullen, Chairman of the Board of the National Association of Blue Shield Plans, Dr. Russell B. Carson—a letter which requested information concerning the relationship between the Society and CMS—it was felt that the Secretary of HEW should be informed that no relationship at all exists between the two organizations at present; that the Council is concerned lest the admittedly substandard payments offered by CMS under its service benefits contracts be interpreted by anyone as being "prevailing" fees in our state; that the Society has good, though informal, working relationships with most of the private carriers through the Health Insurance Council; that the Society is not sufficiently informed as to what coverage and terms will be offered by any insuring agency to express a preference; and, finally, that our door is always open to any company that wishes to present its proposal for examination and/or enlist our support.

Dr. Cullen was asked to transmit this information to Secretary Gardner and, as well, to write a similar letter to Dr. Carson in which he would document in considerable detail the course of events leading up to our split with CMS in 1964, and also define the minimal terms on which the Society would consider resuming sponsorship of that agency.

I imagine that many of our members would welcome the assumption of functional liaison between the Society and CMS—if the terms were right, and, in fact, the Board of Directors of the Hartford Association recently inquired of the Council whether explorations toward that end might not be of value. Pointing out—quite correctly—the influence of medical practice that Medicare and other legislation is bound to have, the Hartford Directors voiced the opinion that the Society and its members might benefit appreciably from liaison, *with some element of voting control*, could be re-established with Connecticut Medical Service. The reply of the Council to this inquiry will be to furnish the HCMA Board with copies of Dr. Cullen's letters to HEW and the National Blue Shield, and to give assurance that the Society stands ready at any time to discuss "matters of mutual interest" with anyone; but, further, to recall that it was the very "element of voting control" in CMS which apparently

could not be resolved in 1964, when sponsorship came to an end.

(e) *Part B—Separate Billing of Patients by Hospital-Based Specialists*

As you know, the Medicare Law excludes coverage of the services of the hospital-based specialists from Part A—the hospital benefits program, and provides that they may be included under Part B contracts—specifically as doctor-care services. At a special meeting of the Council on October 17—a Sunday, by the way—the members were in agreement that the Society should support the positions taken in this regard by our own Sections on Radiology, Pathology, Anesthesiology and Physical Medicine, when and if such positions were made known.

You have before you in your Handbook a resolution received from the Section on Radiology, along with two related resolutions recently adopted by the Council. On Monday of this week, our Section on Pathology also introduced an identical resolution for your consideration and action today. I think we should all realize that while it is the Medicare Law that opened the door on this question, the positions now being drafted by most of the national and state organizations of the four specialties encompass not just the over-65's but *all* patients to which these practitioners render services.

(f) *The Journal Supplement on the Professional Implications of the Medicare Law*

I hope you will all read carefully—and encourage your colleagues to do likewise—the assessment of the professional implications of Medicare which was mailed out with the November issue of *Connecticut Medicine*. Prepared by our General Manager and edited by Dr. Max Caplan's Ad Hoc Committee on Medicare Planning, the Council shares the opinion of the Committee on Hospitals and many physicians throughout the country that this is, indeed, a most timely document and one which uses a refreshingly different approach to making P.L. 89-97 more understandable to the medical practitioner. As the rules and regulations of Medicare become known, the Council plans to try to keep the membership informed through the medium of similar publications. We hear a great deal about "peace through understanding" these days, and certainly this Law needs a maximum amount of the latter if doctors are to bring themselves to live with it peacefully.

## 9. Recommendations Of The Council

Over and above approval of the 1966 Budget, the interim committee appointments, and the resolution on separate billing, the Council has three other recommendations to make at this meeting. Two of these are listed in your Handbook; i.e., authorization to form a Section on Pediatrics and authorization to form a Section on General Practice.

The third is one that the members of the Council are distressed to have to make. One of our distinguished state officers, and a man who has contributed greatly to the work of the Society for many years, has found it necessary to step down from his present post. With great reluctance, just prior to this meeting, the Council accepted the resignation of Jachin B. Davis, of New Haven, as Vice-Speaker of the House of Delegates. To replace Dr. Davis in this office, the Council has appointed Dr. Henry Caplan of New Haven as Vice-Speaker until the next meeting of the House (which

is today), and recommends that this House confirm this appointment for the balance of Dr. Davis' unexpired term.

#### 10. Conclusion

I recognize that this report has been necessarily lengthy but, even so, I would be remiss in my duty if I did not acknowledge the assistance your reporter has received from his fellows in the Council and the staff at St. Ronan Street. Little, if any, progress could have been made without the full and unstinting cooperation of all these dedicated people. And so, to our officers, our county councilors, the chairmen and members of innumerable committees, and to Mrs. Lindquist, Dr. Richards and their able co-workers—my sincere thanks.

Respectfully submitted,  
STEVENS J. MARTIN, M.D., *Chairman.*

#### REPORT OF THE SECRETARY

MR. SPEAKER, MR. PRESIDENT, MEMBERS OF THE HOUSE OF  
DELEGATES AND GUESTS:

One of the few duties assigned to the Secretary of the Connecticut State Medical Society is to keep tabs on the number of members currently enrolled and, while I am not called on to make a numerical report at this session, I am pleased to note that our ranks continue to swell at the rate of about 150 new physicians each year.

It is often said that in numbers there is strength, but, while this is undoubtedly true, I think that the strength of the medical profession in the difficult times ahead must be derived from sources other than merely adding names to our roster. Efforts must also be made to increase the participation of doctors in their own affairs, and it is encouraging to learn of the efforts currently being made by our component county associations toward this end. Indoctrination programs for prospective members have been instituted by several and, from all accounts, are highly educational and being well-received. At least three associations have voted to make minimal attendance at meetings a condition of membership and, although this requirement is still felt by some to be pretty controversial, I am told it is resulting in turnouts of standing-room-only proportions—and that is certainly a condition to be welcomed.

We hear a great deal about "consensus" these days, and it is my feeling that this is as proper an objective for physicians to strive for as it is for politicians. Despite a limited amount of critical expression to the contrary, a meaningful consensus of opinion is what the House of Delegates of the American Medical Association seeks to arrive at through the medium of receiving, debating, and finally acting upon literally dozens of resolutions emanating from the grassroots of medicine—from the fifty states and several territories. When the various local views presented are found to differ, either in kind or in degree, every attempt is made to establish policies which will be acceptable to the majority and, at the same time, will not bring injury or embarrassment to the minority.

Turning now to state level, I trust you will note—as I have—that in the agenda before you today there is a distinct dearth of resolutions emanating from *our* eight component associations—in fact, that there is but a single one. Yet I cannot bring myself to believe that this apparent scarcity of county-oriented opinion means that none exists or that we are all so much in accord with each other on all matters

that there is really nothing worthy of our joint consideration. The occasional adverse local—and sometimes vocal—reactions to decisions of the Council bear out my disbelief that this could be so.

For this reason, among others, it is my judgment that much more could and should be done to strengthen and further implement liaison between the county medical associations and the state medical society so that we doctors in Connecticut may do everything possible to arrive at a sound consensus and promote a stronger unity of purpose toward the problems which beset us currently and the new ones which some of our legislators are promising to beset us with next year and thereafter.

I therefore respectfully present a recommendation to the House of Delegates today with a request that it be given careful consideration and—if you will—approval.

My recommendation is:

That the House of Delegates of the Connecticut State Medical Society request the President, in consultation with the other officers and the General Manager, to arrange and hold a "Conference of CSMS and County Medical Association Officers" at least once each year, for the purpose of seeking to define common goals and interests in the several county areas, implementing programs designed to obtain the grassroots opinions of members on these goals and interests and to convert such opinions into sound policies having statewide application through the medium of actions to be taken by this House of Delegates.

In conclusion, I wish to commend to your attention and perusal the excellent assessment of the professional implications of the Medicare Law which was mailed out with the November issue of the Journal. I think I am divulging no secret by congratulating our General Manager, Dr. Richards, on his authorship of the document. On request, some six hundred copies have already been mailed to individuals and groups of physicians in practically every section of the country—appropriate recognition, it seems to me, of its timeliness and of the fact that it makes good sense even to many of our colleagues who are not fortunate enough to practice medicine in the Nutmeg State.

Thank you.

Respectfully submitted,

WALDO E. MARTIN, M.D., *Secretary.*

#### 1966 MEETINGS

**March 24**—182nd Annual Meeting of the New Haven County Medical Association to be held at the Waverly Inn, Cheshire, Connecticut. Business Meeting tentatively set for 3:30 P.M.

**April 26-28**—174th Annual Meeting of The Connecticut State Medical Society to be held at the Statler-Hilton Hotel, Hartford, Connecticut.



# FROM THE GENERAL MANAGER'S OFFICE

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## SUMMARY OF ACTIONS COUNCIL MEETING

Thursday, December 9, 1965

### I. Attendance

Present in addition to the Chairman, Dr. S. J. Martin, were: Drs. Cullen, Hess, Bradley, Goldberg, W. Martin, Weise, Sr., M. Caplan, Gardner, Brandon, Pitock, Grendon, Egan, H. Caplan, Spitz, Palumbo, Shepard, Ayres, Nolan, Cramer, Fabro, Abbot, Petrie, Wilson, Hastings and Roch. Also present were: Mrs. Lindquist, Mr. Burch, Mr. Chilcoat (AMA) and Dr. Richards. Absent were: Drs. Davis, Rogol, Ciccarelli and Epstein.

### II. Routine Business

#### Approval Of Minutes

As printed and distributed, it was VOTED to approve the minutes of the meeting of November 17, 1965.

#### Introduction Of New Associate Councilor

The Chairman introduced Dr. Edward Palomba of Somers as the new Associate Councilor from Tolland County to replace Dr. John Hughes, resigned.

#### Committee Appointment

*Advisory Committee to State Commissioners of Welfare, Finance and Control:* Having received notice from Clifford Joseph, Torrington, that he does not wish to accept service on this Committee, it was VOTED to appoint J. Harold Root, Jr., Waterbury, to replace J. Harold Root, Sr., Waterbury, whose resignation was accepted at the last meeting.

#### Report—AMPAC Conference

Kenneth F. Brandon, Hartford, filed a report with the Council on the proceedings of the American Medical Political Action Committee Conference, Chicago, November 5, 1965. It was VOTED to accept Dr. Brandon's report as information.

#### Representatives—Planning Committee On

##### Hospital-Acquired Infections

At the request of Dr. James C. Hart, Director of the Preventable Disease Division, State Department of Health, it was VOTED to appoint two repre-

sentatives of the Society to serve with a "planning committee" being set up by Dr. Hart to arrange for conducting a seminar on hospital-acquired infections in Connecticut. The first meeting of the seminar will be held in Dr. Hart's office at 10:00 A.M. on January 19, 1966. It was further VOTED to request Stanley H. Osborn, Chairman of the CSMS Committee on Public Health, and Max Caplan, a member of the Committee, to serve as the Society's representatives to this project.

#### Date Of Next Meeting

The next meeting is scheduled to be held on Wednesday, January 26, 1966.

### III. Old, New And Special Business

#### Resignation And Replacement—Vice-Speaker Of The House Of Delegates

Having been informed that Jachin B. Davis, New Haven, declines to reconsider his decision to resign as Vice-Speaker of the House, it was VOTED to remove his October 29 letter from the table, and it was further VOTED to accept, with regret, his resignation from office. Subsequent to this action, and by closed ballot, Henry Caplan, Meriden, was elected to be appointed by the Council as Vice-Speaker in Dr. Davis' place, and it was VOTED to recommend to the next meeting of the House of Delegates that his appointment be confirmed to complete Dr. Davis' unexpired term (to April 26, 1966) in that office.

*N.B.*—At its semi-annual meeting on December 9, 1965, the House of Delegates confirmed Dr. Caplan's appointment as Vice-Speaker.

#### Reactivation—Committee On Relative Value Study

At the recommendation of the Commission on Third Party Payments, it was VOTED to request Stewart P. Seigle, Hartford, Chairman of the Committee on Relative Value Study, to reactivate the Committee for the purpose of reviewing the over-all experience of members, sections, committees and others with the use of the Relative Value Schedule since its adoption in April, 1965; to obtain and evaluate recommendations from the various sections and groups concerning suggested changes in the unit values for selected services; and to make a report with recommendations to the Council for

transmission to the House of Delegates at the Annual Meeting on April 26, 1966.

#### **Authorization—Committee On Third Party Payments**

At the request of the Chairman of this Committee, Howard K. Ente, Westport, it was VOTED to authorize the Committee to spend up to \$200, if necessary, for the purpose of consulting with one or more cost-analysis agencies to determine whether it is practical (probably on a sample basis) to define "the cost to physicians of supplying medical services."

#### **Designation Of "Intermediary"—Part B Of Medicare**

It was VOTED to receive as information a letter from Mr. John A. Hill, President of the Aetna Life Insurance Company, to CSMS President James R. Cullen, in which Mr. Hill informed Dr. Cullen that Aetna has applied to HEW to be designated "fiscal intermediary for Medicare (Part B) in Connecticut and expressed the hope that, if selected, his Company could count on continued "excellent relationships with the Society" and could depend on "the good will and cooperation of the medical profession." It was further VOTED to send to the chairman of the Connecticut chapter of the Health Insurance Council, as information, a copy of the letter Dr. Cullen wrote to the Secretary of HEW concerning the Society's unwillingness to express any preference for any agency, at this time, although its doors remain open to discuss the matter "with responsible representatives of government and/or insuring agencies" and "to evaluate any proposition advanced by either to establish an acceptable Part B program in Connecticut."

N.B.: *The foregoing is a summary of the proceedings and actions of the Council on December 9, 1965. Detailed minutes of the meeting are on file at 160 St. Ronan Street, New Haven, for perusal by any interested member of the Society.*

#### **PLACEMENT WANTED**

**DERMATOLOGIST** — Broad background and extensively trained Dermatologist seeks group association, position or desirable practice location upon completion of residency in June, 1966.

**GENERAL SURGEON** — Board eligible, excellent background in general surgery with sub-specialty in neo-plastic surgery. Available immediately, with willingness to go into General Practice, as well as surgical practice. Military obligations completed.

**GENERAL SURGEON**—Board eligible, 35 years of age, military obligations completed. Would like to practice with a partner or group. Has sub-specialty of thoracic surgery. Available January 1.

**GENERAL SURGEON** — Board certified, sub-specialty in Head and Neck Surgery. Especially interested in Derby-Ansonia and Danbury areas of Connecticut.

**OBS-GYN**—33 years of age, Board eligible, military obligations completed. Interested primarily in association with another Obs-Gyn. Available as of January 1.

**INTERNIST** — Board certified, interested in relocating in Connecticut in a medium to large community with either a group of partner. Military obligations completed, available within a very short period of time.

**INTERNIST**—35 years of age, Board eligible, Connecticut license. Sub-specialty training in Gastroenterology, Endoscopy, Small Intestinal Biopsy. Wishes to associate with an established physician or medical group.

**INTERNIST**—Board certified, 33 years of age, military obligations completed. Would like to practice in a medium or large community. Primarily interested in an association or group practice, but will consider individual openings, as well. Available as of January 1.

**OBS-GYN**—Board eligible Obs-Gyn with Connecticut license wishes to locate in practice in Connecticut with either a partner or group. Will consider solo practice, also. Available immediately.

#### **PLACEMENT OPPORTUNITIES**

**ANESTHESIOLOGIST** — Board certified or Board eligible Anesthesiologist to serve in 65 bed, fully accredited rural hospital which takes care of two communities of about 40,000 total population.

**INTERNIST** wanted for expanding medical group in urban area of Connecticut. Call or write: Chapel Medical Group, 1308 Chapel Street, New Haven, Connecticut.

**WANTED** — A young practitioner trained in General Medicine and Pediatrics to share fully established practice. Two fully accredited hospitals totaling over 700 beds serve the area. Address inquiries to: P. O. Box 469, Woodbury, Connecticut.

**INDUSTRIAL PHYSICIANS** — Two physicians qualified in Internal Medicine with some knowledge of Surgery for two large, respected national corporations to serve on corporate staff. These firms are located in Hartford, Connecticut area. Regular hours, 38 hour week, salary range \$16-\$18,000 plus full benefit program.

G.P.s needed for the Meriden-Wallingford area for private practice. For further information, contact: M. J. Esposito, M.D., 335 Cook Avenue, Meriden, Connecticut.



# 1965: More Understanding In Genetics; Progress Against Leprosy; A VD Campaign; Medicare

■ Scientists who try to understand life by studying its lowest common denominators made some important advances in 1965.

No one can yet answer the question: What is life? But this year, for the first time, scientists put together a synthetically-produced model of a nucleic acid—one of the lowest common denominators—and saw it reproduce itself in the test tube.

Other major news stories in biology and medicine this year included:

- The first determination of the complete chemical structure of a nucleic acid.

- Cultivation of the leprosy bacillus in tissue culture for the first time, an advance that can mean much for investigators trying to develop medicines to prevent or combat the disease.

- The apparent implication of a virus or other cancer-causing agent in leukemia among several members of the same family. Viruses have been implicated in certain animal leukemias but their role in the human form of the disease has never been clear.

- A unique research facility, the Institute for Biomedical Research of the American Medical Association Education and Research Foundation, officially opened its doors. Dedicated to basic scientific investigation, its members look for new questions rather than answers to problems already defined.

- The American Medical Association opened a campaign against venereal disease, the nation's most urgent communicable disease problem.

- Two controversial pieces of legislation—medicare and the regional medical center bill—were signed into law.

The first synthesis of a self-reproducing component of living matter was achieved at the University of Illinois Center for Advanced Study.

Sol Spiegelman, Ph.D., and co-workers assembled a self-propagating, infectious ribonucleic acid of the bacterial virus Q-beta. Ribonucleic acid (RNA) is one of the complex chemicals on which the heredity of living organisms is coded; the other is deoxyribonucleic acid (DNA). Virus Q-beta, one of the group of viruses called bacteriophage because they attack bacteria, is an organism whose genetic coding is carried on RNA.

(In most living organisms the basic genetic code is DNA-borne and RNA acts as a messenger between the DNA master plan and the cell machinery. As far as is known, RNA carries the master plan only in some viruses. The nucleic acid in a virus is surrounded by a protein coat. When a virus attacks a bacterial cell it leaves the protein coat outside after "injecting" the nucleic acid. The viral nucleic acid takes over the genetic machinery of the cell and uses it to direct the cell to produce more viral nucleic acid and viral protein coats. Eventually, the cell disrupts, spilling the assembled viruses into the extra-cellular environment where they can attack more cells.)

Dr. Spiegelman and his group said the key to the synthesis was a purified enzyme, a chemical that takes part in chemical reactions but is not changed itself.

The enzyme, RNA-dependent-RNA-polymerase ("replicast" for brevity) was induced in the bacteria *Escherichia coli* by infecting the cells with virus Q-beta. Replicase is a natural product of virus Q-beta infection; it is the "runner" which helps to assemble copies of viral nucleic acid according to viral RNA instructions in the invaded cell. Purified enzyme was then mixed with RNA from Q-beta virus and component chemicals of which RNA is made. No bacterial cells were present in the mixture and no virus.

With the viral RNA acting as template or pattern, the enzyme assembled component chemicals into new strands of RNA. Subsequent experiments proved that the synthesized RNA was as competent as viral RNA in acting as a template for the formation of still more synthesized nucleic acid.

To complete the proof that the synthesized RNA was identical to the original viral RNA, experiments were conducted which showed that virus particles produced by the synthetic RNA were of the same serological type as authentic Q-beta.

Explaining the significance of the work, aside from the fact that synthesis of nucleic acid was actually achieved, Dr. Spiegelman said:

"For the first time a system has been made available which permits the unambiguous analysis of the molecular basis underlying the replication of a self-propagating nucleic acid. Until now we

searched indirectly. It was like fumbling inside a black box. Now we can know what to do."

Dr. Spiegelman predicted that methods soon will be developed to permit the synthesis of self-replicating DNA.

Another group of scientists at Cornell University, Ithaca, N. Y., succeeded in determining the structure of an RNA molecule. Knowledge of the chemical structure of a nucleic acid is critical information: the repeated occurrence of certain chemical bases in the molecule comprises the "code" for the genetic information carried by that specific nuclei acid.

In this case the nucleic acid was alanine-specific transfer RNA. In non-chemical terms, that means the nucleic acid is a form of RNA which operates under DNA instructions, transferring the amino acid alanine to a point in the cell where amino acids are assembled into proteins.

Using alanine-specific transfer RNA isolated from bakers yeast, Robert W. Holley, Ph.D., and fellow investigators determined that the nucleic acid is made up of 77 bases and described the order in which the bases occur.

A London, England, scientist breached one of the last barriers to faster development of anti-leprosy drugs or preventive agents. The leprosy bacillus, *Mycobacterium leprae*, was grown in tissue culture by Elizabeth Garbutt, M.D., of the British National Institute of Medical Research.

Development of therapeutic and prophylactic agents has been slowed by the inability of investigators to grow the bacillus experimentally. Cultivation of a disease organism in the laboratory enables medical scientists to test its sensitivity to various drugs. Work toward development of a vaccine requires a supply of laboratory-grown organisms.

The laboratory-grown bacilli of Dr. Garbutt proved to be infective when injected into the footpads of mice, opening the way for their use in medical research. Sometimes laboratory cultivation "tames" a disease organism to the point where it is noninfective.

The leprosy bacillus, discovered in 1874, was one of the last agents associated with a worldwide disease to remain uncultured. Leprosy probably afflicts about 10 million people in the world.

A disease that remains largely cloaked in mystery is human leukemia. More than any other cancer, viruses seem implicated in its cause and yet proof of a viral etiology is still lacking. Heredity sometimes seems to play a role, too: leukemia is sometimes observed to "run" in families. Viruses are the proven cause of some animal leukemias.

In 1965, for the first time, a cancer-causing agent that may be a virus appeared to have been implicated in the production of human leukemia.

Presumptive evidence of the agent was found in a family where an abnormal chromosome (known as the Philadelphia chromosome) was detected in: (1) a grandfather who recently died of chronic myelogenous leukemia; (2) his daughter, and (3) two grandchildren. Neither the daughter nor grandchildren have the disease but chronic myelogenous leukemia is believed to have claimed the lives of the dead man's father, brother, sister and a nephew.

Chromosomes are the X and Y-shaped cellular bodies that carry the genes of heredity. The Philadelphia chromosome, seen only in persons with chronic myelogenous leukemia, is an abnormal body with part of one arm missing.

A nongenetic, transmissible agent—perhaps a virus—may be responsible for the abnormal chromosome in this family, according to the investigator who reported the work, Kurt Hirschhorn, M.D., assistant professor of medicine at New York University Medical Center.

Why does Dr. Hirschhorn believe that a virus or similar agent is operating in this family rather than some genetic factor?

According to his explanation:

Chromosome analyses were made of members of the family after the high familial incidence of chronic myelogenous leukemia was noted by Leo Weiner, M.D., Bronx Veterans Administration Hospital. Virtually all the white blood cells in the grandfather's bone marrow (where blood cells are produced) carried the Philadelphia chromosome although the abnormal chromosome was absent in other cells. In the healthy daughter and two healthy grandchildren the Philadelphia chromosome was found in only 10 to 15 per cent of the white blood cells—a percentage one would not expect to find if development of the Philadelphia chromosome was genetically determined.

What appears to have been transmitted from parent to offspring was a nongenetic tendency for the abnormal chromosome to occur. Dr. Hirschhorn pointed out that: (1) the Philadelphia abnormality is apparently caused by deletion of one arm of the chromosome, and certain viruses are known to cause chromosomal aberrations in tissue culture; and, (2) transmission of leukemia virus is known to occur between female mice and their offspring.

Whether the healthy daughter and grandchildren will eventually develop chronic myelogenous leukemia is a question that will be answered only with time—perhaps 30 years—since the disease characteristically has a late onset. Whether or not the disease develops, said Dr. Hirschhorn, may depend upon the ability of each person's body to maintain an internal environment hostile to cells containing the abnormal chromosome.



A new anti-rabies virus vaccine cultured in human cells in tissue culture was continuing under development during 1965. Scientists at Wistar Institute, Philadelphia, have been conducting animal experiments with the vaccine for about three years. High levels of rabies antibody and excellent protection against rabies virus have been obtained in mice, guinea pigs, dogs and monkeys. Both live and killed-virus vaccines have been tested.

In animals, only one to three inoculations of the live-virus vaccine have been necessary to produce immunization against rabies. In many animals, a good antibody level was obtained within seven days.

A rabies vaccine that achieved the same results in human beings would be a boon to rabies victims, who at present are subjected to a series of at least 14 daily injections of vaccine.

The practicality of hypnotizing persons via television was demonstrated by two psychiatrists at the Columbia University College of Physicians and Surgeons. Warning of the dangers of the technique in the hands of unscrupulous operators, they said the experiment emphasized the need to maintain safeguards and control over persons having access to public broadcasting systems.

Investigators Herbert Spiegel, M.D., and James H. Ryan, M.D., reported on the work in June at the Annual Convention of the American Medical Association.

The experiment, they said, was carried out with the voluntary cooperation of two subjects who were known from previous experience to be hypnotizable. In each case, the subject was seated in an empty room with a television receiver. While medical monitors watched through an observation system, the hypnotist's image appeared on the screen, spoke to the subject, and made hypnotic signals.

The induction of a trance and the implantation of a post-hypnotic paralysis in both subjects was taken as evidence that the experiment succeeded in proving the possibility of hypnosis via television.

The Food and Drug Administration, upon the recommendation of physicians, proposed tighter restrictions on the non-prescription use of vitamin D.

Vitamin D is one of the fat-soluble vitamins, which, unlike the water soluble, can be stored in the body. Thus, a continuous high intake of vitamin D might result in an oversupply and possible bodily harm. Some medical investigators have linked excessive vitamin D to hypercalcemia, an excess of calcium in the blood which in its severe form may produce abnormal changes in tissues. In certain diseases a high intake of vitamin D may be prescribed by a doctor; the FDA proposal is aimed at reducing vitamin D intake through "forti-

fied" foods and self-dosage with vitamin supplements.

Advisory committees of the American Medical Association and American Academy of Pediatrics told the FDA that, while there is no positive demonstration of a cause-and-effect relationship of vitamin D to hypercalcemia, there should be restrictions on vitamin D made available to the public through supplemental foods or vitamin preparations. Both committees pointed out that an excessive intake of vitamin D, even if not harmful, is certainly of no value. The recommended daily intake of vitamin D for healthy adults is 400 international units, which is normally supplied in a good diet.

The laboratories of an important new research facility opened for business with the dedication of the Institute for Biomedical Research of the American Medical Association Education and Research Foundation.

The purpose of the Institute is to provide a privately supported basic research facility of excellence in which the investigator-members may devote their interests to work without any other duties except as they may elect. As such, the Institute is a manifestation of the recognition, interest and support given to basic research by the American physician.

Recognizing that biology is the study of the life processes, and that diseases are aberrations of these processes, the Institute is devoted to the support of fundamental inquiry into the life processes on all basic levels. It does not focus attention on disease-oriented programs except to aid the individual scientist in research. The Institute undertakes no dictated research activities or applied research. A typical area of Institute interest is molecular biology, including experimental ecology, biochemical genetics, and antibody synthesis.

Director of the Institute is Roy E. Ritts, Jr., M.D. Investigators appointed to the Institute as of November 1 are Howard A. Schneider, Ph.D.; Clyde R. Goodheart, M.D.; Dan W. Urry, Ph.D.; and John J. Cebra, Ph.D. George R. Collins is director of the Institute's Animal Research Facility.

Dr. Schneider will continue to work with a disease resistance factor, which he calls pacifarin, found as a contaminant in certain foods. Twenty years of investigation have convinced Dr. Schneider that the pacifarin compounds are in reality a group of previously unknown entities that may be among the most potent disease inhibitors ever found.

Even a microscopic amount of a pacifarin extracted from wheat or dried egg white will protect mice against infection by mouse typhoid bacteria. Although mouse typhoid is the only disease for which a pacifarin has been found, Dr. Schneider

believes that there are other pacifarins capable of preventing other diseases.

The American Medical Association also moved in 1965 to implement its first statement on population control since 1938. In late 1964 the AMA House of Delegates adopted a position that "the prescription of child-spacing measures should be made available to all patients who require them, consistent with their creed and mores, whether they obtain their medical care through private physicians or tax or community-supported health services."

The previous AMA statement said such measures should be given "only in dispensaries, clinics and similar establishments licensed to treat the sick and under medical control."

The new policy statement says that the subject of reproduction and birth control is a matter of responsible medical practice as well as responsible parenthood. It urges the medical profession to accept a major responsibility in matters related to human reproduction as they affect the total population and the individual family. Doctors are told they must be prepared to provide adequate counsel and guidance when the needs of the patient require it. A manifestation of the new policy appeared in the *Journal of the AMA* in October, 1965, in the form of a medical evaluation of all known contraceptive methods. Prepared by physicians and adopted by the AMA Committee on Human Reproduction, the evaluation of contraceptive methods was designed to aid the physician in patient counseling.

A major addition to adverse drug reaction reporting programs was set up through cooperation of the American Medical Association, Pharmaceutical Manufacturers Association, and the Food and Drug Administration.

The Registry of Tissue Reactions to Drugs was established within the Armed Forces Institute of Pathology in Washington, D. C. Its purpose is to obtain autopsy or biopsy material from patients with suspected drug reactions. Examination of the material is carried out by a resident pathologist and consultants in pathology and toxicology, after which the material is stored for possible future research. Results of tissue studies are sent to local pathologists who furnished the study material. Each of the three sponsoring organizations receive monthly summary reports.

The Tissue Registry augments existing drug reaction reporting programs maintained by the AMA and FDA, and provides an opportunity for more definitive study of reactions in individual persons. The unique cooperative effort involved in setting up the Tissue Registry is the first between major drug manufacturing, drug prescribing, and drug regulating bodies.

Medical and public health organizations opened a campaign against venereal disease, noting that VD is now the Number One communicable disease problem in the United States. VD has been on the increase especially among young men and women, the American Medical Association said in opening its campaign.

Part of the problem is due to complacency about VD which developed after World War II; because penicillin proved effective in knocking out most cases quickly, it was assumed by many persons that venereal disease would soon be wiped out altogether.

Complacency was shattered by: (1) an increase in penicillin-resistant strains of certain VD organisms; and, (2) a rising VD rate, especially among teen-agers, who often do not seek treatment out of ignorance or fear of exposure.

The AMA campaign consists primarily of alerting the public and the medical profession to the hazard of VD.

Only July 30, President Johnson signed H.R. 6675, the medicare bill, into law. The \$6.5 billion program to provide hospital insurance and health care to the elderly through a federalized system was approved by a 307-116 vote in the House of Representatives and a 70-24 vote in the Senate. Medicare becomes effective July 1, 1966.

Officials of the American Medical Association, which had opposed such legislation, met with the President and officials of the federal Department of Health, Education and Welfare to discuss the development of rules and regulations.

One provision of the medicare bill to which the AMA and other medical organizations strongly objected was the proposed inclusion of the professional services of radiologists, anesthesiologists, pathologists and psychiatrists under the hospitalization portion of the legislation. The final version of the bill, agreed upon after a House-Senate conference, did not include the four specialties under the hospital care section.

Early in the year, the President's Commission on Heart Disease, Cancer and Stroke, a panel of 28 persons named by President Johnson in 1964, issued a report recommending a nationwide program to combat the three diseases.

After Congressional hearings and a conference with officials of the American Medical Association, legislation was drafted and voted which met some of the objections of the AMA and other opponents of a program on the scale envisioned by the President's Commission report.

The recommendation of the report covered medical research, education and practice, and contemplated spending \$3 billion in five years, plus an undetermined amount in state and other spend-



ing. The key recommendation, accounting for more than half the \$3 billion, was for creation of a national network of centers for patient care, research and teaching in the three disease areas. The AMA said such a program could weaken the present structure of medicine through over-emphasis on certain diseases and certain segments of medical research and medical-health care.

The bill finally voted by Congress and signed by the President reduced the program in scope and categorical emphasis, approving the spending of \$340 million over three years.

It provides grants to set up regional cooperative arrangements among medical schools, research institutions and hospitals for research and training and for related demonstrations of patient care in

the fields of heart disease, cancer, stroke and related diseases.

The program is to be carried out "in cooperation with practicing physicians, medical center officials, hospital administrators, and representatives from appropriate voluntary health agencies."

Federal grants are limited to planning activities, feasibility studies, and remodeling and renovation of buildings and replacement of obsolete equipment. No new construction is allowed.

Aim of the legislation, according to the Administration, is to afford the medical profession and medical institutions the opportunity of making available to their patients the latest advances in the diagnosis and treatment of heart disease, cancer, stroke and related diseases.

*Reprinted from the American Medical Association.*

## **CONNECTICUT 65 PLAN TO TERMINATE PRESENT COVERAGE FOR ELDERLY**

*(Thanking the Society for its "assistance in originating Connecticut 65," Mr. William N. Seery, Chairman of the plan's Executive Committee, asks that "sincere appreciation be passed along" to the members of the Society for their cooperation during the past four years.)*

Connecticut 65, the pioneer plan to provide major medical health insurance protection for elderly residents of Connecticut, will terminate its coverage July 1, 1966, the date on which the federal Medicare program becomes effective.

In a letter to each of the 27,000 subscribers to the plan William N. Seery, Chairman of the Associated Connecticut Health Insurance Companies which underwrite Connecticut 65, pointed out that on that date the purpose for which Connecticut 65 was established will no longer exist. Many of the expenses covered under the Connecticut 65 plan will be covered under the provisions of the federal program.

"Some of our subscribers—spouses of subscribers 65 years of age or over—are under 65," Mr. Seery pointed out. "Medicare benefits will not be available to them until they become 65. However, provision will be made to offer coverage for all those in this category, and details will be released in the near future."

The letter to the subscribers urges them to continue their Connecticut 65 coverage until July 1, 1966 "right up to the hour when Medicare begins."

While Connecticut 65 will terminate its coverage on July 1, it will continue to stay in business after that date to pay outstanding claims, in accordance with the provisions of the policy, for covered expenses incurred as a result of an accident or illness occurring prior to July 1, 1966.

Connecticut 65 started on October 1, 1961. Since that time more than 70,000 checks, totalling more than \$12,000,000, have been issued to help Connecticut residents over 65 meet the costs of severe illnesses or accidents. Over 42,000 persons have been enrolled in the program.

Mr. Seery said, "Up to the time that Connecticut 65 was organized it was difficult, if not impossible, for elderly persons to get major medical insurance without medical or physical examinations. Companies had to explore a whole new and untested area of health insurance and initiate legislation to permit the companies to join together to offer the plan."

He points out that the Connecticut plan became a model for many similar plans in other areas of the country.

## REPORT ON DISASTER MEDICAL CASE

(On November 17, 1965, the Council voted to publish the following report in the Journal for the information of physicians.)

With the permission of the Council of The Connecticut State Medical Society I attended the meeting of the O C D Regions 1 and 2 of the Committee on Disaster Medical Care of the Council on National Security, American Medical Association. The meeting was held in Washington, D. C. on August 7 and 8, 1965. The purpose of this conference was to promote and assist in the development of state and local programs of medical preparedness for disaster.

States from the eastern seaboard were represented at the meeting. These states were Connecticut, Pennsylvania, District of Columbia, Maryland, Maine, Massachusetts, New Hampshire, New Jersey, New York, Ohio, Rhode Island, Vermont, Virginia, West Virginia, and Delaware. Progress reports were given by a representative from each of these states concerning the various activities of the represented states. Most of the reports dealt with blood banks and their functions in disaster, stock piling of supplies, and courses on mass casualty care. Several of the states, namely Maine, New Jersey and Connecticut have already begun an inter-hospital intra-state radio network. In Maine this network is now incorporated into the State Police radio network.

The role of the Military in Disaster Planning and Operations was discussed by Dr. Shirley Biss. He stated that civil defense is a civilian responsibility. There are civil defense coordinating boards at eight regional levels. Coordinated planning and supply should be done by the military under the direction of the adjutant general of each state. If mobilization should take place the Army would provide advice and help to civil defense. Dr. Biss stated that there is a two hundred bed hospital in Tupper Lake, New York which is used by the Army for exercising and training of reserve units in civil defense.

The Army Medical Plan notes a preposition of war reserve stocks in the following categories: 1. Material for collecting blood. 2. Material for treatment of fallout in water and for preserving water supplies. 3. Supplies of cots and beds, etc. 4. Shelters.

Dr. Biss stated that the Navy planning was directed to a war created disaster, and the Navy would coordinate its activities with all other services. Wherever Navy activity is present, a disaster control team is a part of that activity.

Mr. Arnold H. Dodge of the U. S. Public Health Service mentioned the fact that the budget for the Division of Health Mobilization was zero. However, Funds were available from other sources.

Discussion of the Packaged Hospitals for civil defense revealed that training units were now made so that the entire unit weighed 8,000 lbs., was more easily moved, and unpacked. This unit contained training kits, films, and expendable supplies.

Col. L. J. Hackett, Jr., MC. USA, Medical Advisor, from the office of the Secretary of Army, discussed civil defense and stated that martial law is not acceptable as a base for planning. There are now 550 task forces mobilized for civil defense. He stated also that development of defense plans at state level is moving well. He said that management of key resources in disaster is at federal, state, and local levels. The resources plan is being brought up to date and that the Health Resources Advisory Committee is being revised. There are thirty-four million shelter areas available but he did not state how well they were supplied.

The California Flood Disaster of December, 1964, and January, 1965, was discussed by Dr. Wayne P. Chesbro. He stated that no typhoid vaccine was available, but that tetanus boosters were given. He emphasized that a mobile disaster unit should be available during a disaster. They had great difficulty procuring physicians to go to the disaster area to take care of the injured and ill. Dr. Chesbro stated that at the command post level there was a lack of knowledge of the true disaster problems. He noted especially that personnel have to be cognizant of daily progress and a log and accurate statistics should be kept. Roster of physicians for emergency services should be kept and that this roster could be used for interstate emergencies.

Col. John H. Trenholm of U.S. Air Force spoke on a MUST Hospital Unit which is a new type of mobile hospital unit, and showed slides illustrating this.

The MEND Program was also discussed. It was stated that the federal government will give teaching grants to schools for MEND. It was noted that medical schools with a MEND Program were carrying out disaster drills which in some schools included the first year student.

A panel consisting of a state health officer, county health officer, a local physician and nurse discussed



drills and medical emergency preparedness. This panel stated that student nurses should be required to participate in hospital disaster drills and in this way should be prepared for an emergency. The role of the county health officer was discussed, and it was felt that he should report to the State Health Department in event of a disaster. A local physician presented his views on the work of an Emergency Disaster Unit organized in Washington, D. C., sponsored by the District of Columbia Medical Society and controlled by it. The participating physicians in the unit carry a trunk full of equipment including respirators, bandages, surgical instruments, and drugs. The entire panel agreed that the private physician does not participate sufficiently in disaster drills and medicine. The doctors should be made more aware that they have a definite role in disaster medicine.

Dr. Francis C. Jackson summarized by saying that many natural disasters such as fires, floods, tornados, or explosions are a daily threat to our way of living. Physicians should be trained in meeting a disaster as the people in a community look to the physician to take care of their emergency medical needs, and have a right to expect the doctor to be prepared.

Respectfully submitted,

JOHN SHOUKIMAS, M.D.

MARK YOUR CALENDAR —

## **174th Annual Meeting**

**CONNECTICUT STATE  
MEDICAL SOCIETY**

**April 26, 27, 28, 1966**

**STATLER-HILTON HOTEL  
Hartford, Connecticut**

— PLAN NOW AND SAVE THE DATES

## **AROUND THE STATE**

### **Graduate Summer Session Of Statistics In The Health Sciences**

The Department of Epidemiology and Public Health, Yale University School of Medicine, is the host institution for the ninth cooperative Graduate Summer Session of Statistics in the Health Sciences, to be held from June 27 to August 5, 1966.

The Summer Session, under a grant from the National Institutes of Health, is offering courses at nearly every academic and experience level. It is designed to meet some of the educational and training needs of men and women engaged in work in health and health-related agencies, and those preparing themselves for such work.

The courses and instructors for the 1966 Summer Session are: Statistical Methods in Public Health, Hugo Muench, Jr. (emeritus, Harvard); Health Data as Research Resources, Robert Patton (N. Y. State Dept. Mental Hygiene, Albany); Biostatistics in the Health Sciences, Theodore Colton (Harvard); Demographic Methods in Public Health, Helen Abbey (Johns Hopkins); Statistical Methods in Epidemiology, Johannes Ipsen (Univ. Penna.); Sampling Techniques in the Health Sciences, Donovan Thompson (Univ. Pittsburgh); Statistical Methods of Biological Assay, C. Philip Cox (Iowa State); Advanced Biostatistics in the Health Sciences, Richard McHugh (Univ. Minn.); Biomathematics, Malcolm Turner, Emory Univ.; Stochastic Processes in Biostatistics and Epidemiology (C. L. Chiang, U. Calif., Berkeley); Mathematical Methods of Statistics, Robert Elston (Univ. North Carolina); Application of Computers in the Health Sciences, Arthur Littell (Western Reserve).

A seminar series will be presented by Professor William Cochran, Harvard University, on "The Planning and Analysis of Non-Experimental Studies."

(Anyone interested in obtaining further information about this program may do so by writing to Professor Colin White, Dept. of Epidemiology and Public Health, Yale University, New Haven, Conn.)

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## Letters To The Editor

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### To The Editor:

I note that the Woman's Auxiliary uses on its seal the Staff of Hermes.

Doctors use the Staff of Aesculapius.  
With whom are the wives fighting?

MICHAEL S. SHEA, M.D.

New Haven, Connecticut

*To which Mrs. Richards replies:*

### To The Editor:

In defense of the use of the Staff of Hermes by the Woman's Auxiliary to the Connecticut State Medical Society:  
Dear Doctor:

The "wives" wouldn't think of fighting with the doctors. After all, the Auxiliary exists only because the members are wives of the doctors. As an Auxiliary we hope to be aides to our doctors, but it would be highly presumptuous of us to assume the rights of the doctors by using their "Staff of Aesculapius" to which they are entitled after years of study and hard work.

The Auxiliary to the American Medical Association uses as their seal the right side only of the Staff of Hermes or Caduceus—"the better half on the right side."

The pin and seal of the Auxiliary to the CSMS was designed by one of the Auxiliary members after consulting Webster's dictionary and finding that the wand of Hermes or Mercury, the messenger of the Gods, is used as a symbol of the medical profession by a number of medical groups including the United States Public Health Service, the Medical Corps of the United States Army, various hospitals and drug companies, the American Cancer Society, and a number of national medical fraternities. The two symbols seem to be in use so commonly that she chose the one that lent itself best to the design.

Sincerely,

FRIEDERIKE H. RICHARDS, *President*  
Woman's Auxiliary to the  
Connecticut State Medical Society

### To The Editor:

I would like to make a point of expressing my appreciation for the fine cooperation of Connecticut physicians in filling out medical reports for patients applying for benefits under the Social Security Disability program.

For the past several years, I have been Chief Medical Consultant of the Bureau of Disability Determination, the Connecticut agency that makes disability determinations for Social Security locally. Reviewing physicians at this agency evaluate a patient's claim, chiefly on the basis of the medical information that the treating physician submits.

Nothing has been more gratifying to me than the excellent fashion in which Connecticut physicians have responded to our request for reports. Their efforts have made it possible for our agency to do an effective job of handling the claims of Connecticut residents.

As you know, the Social Security Disability program pays monthly benefits to disabled workers under age 65 and their dependents. Families can receive as much as \$309 a month. The average beneficiary with a long-term disability receives over \$11,000 from the program. Currently, some 15,600 Connecticut residents are benefiting from the disability program. These figures emphasize the economic importance of the medical reports that Connecticut physicians submit on behalf of their patients.

But physicians participate in the disability program in other ways as well. By advising a disabled patient about the program, they help him secure benefits due him. In fact, were it not for referrals from doctors, a significant number of qualified persons would lose some or all benefits.

Furthermore, physicians help motivate the patient to pursue the opportunities for rehabilitation that the disability program offers.

Finally, by serving on State and national advisory bodies, physicians help assure that administrative procedures are oriented toward the needs of the medical community.

In recognition of the many constructive roles that Connecticut physicians play in the disability program, I offer my compliments. I only wish I could present them personally. They are richly deserved.

Sincerely,

FRANK H. COUCH, M.D.  
Chief Medical Consultant  
State of Connecticut  
State Department of Education  
Disability Determination Unit  
33 Garden Street  
Hartford, Connecticut 06105

**DOCTOR—Does your wife like to read  
the Auxiliary news? Then be sure and take  
your copy home.**

# WOMAN'S AUXILIARY

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Mrs. John Baybutt, Eastern Regional Chairman for AMA-ERF holds State workshop with Mrs. Irving Krall.

As the guest of Mrs. Irving Krall, Connecticut Chairman for AMA-ERF, a workshop for all County Chairmen, your State President and President-Elect was conducted by Mrs. Krall and Mrs. Baybutt at the Tumblebrook Country Club in Bloomfield on Tuesday, December 7th.

Mrs. Baybutt stressed that AMA-ERF "is meeting a need that is unmet and is not competing with any local, statewide, or national programs for loans to medical students or grants to Medical Schools."

Last year all the state Auxiliaries raised \$321,000 for the National Auxiliary's AMA-ERF fund.

From the AMA-ERF fund, ninety-three medical students from Connecticut received loans totaling \$111,000 last year.

The Connecticut Auxiliary contributed \$3,800 to the fund.

Money contributed to the Loan Guarantee Fund of AMA-ERF is held as a guarantee for repayment of loans. Each dollar in the fund puts another \$12.50 to work in loans made by a commercial bank.

Contributions to the Funds for Medical Schools program of AMA-ERF are distributed annually. Money designated for a particular medical college is presented to the school plus an equal share from undesignated funds. Mrs. Baybutt stressed that every dollar contributed to AMA-ERF is used exclusively for its program, the cost of administering the program is paid for totally by the AMA.

The many means of fund raising were discussed. Gold and silver caduceus and state charms, bracelets and other jewelry are available to Auxiliary members through their State AMA-ERF chairman, at a considerable saving plus a generous profit to the fund.

Note paper is offered from national headquarters in three colors, white, pink and blue (the entire

cost being met by the AMA) and sold by county and state AMA-ERF chairmen for a 100 per cent profit.

Christmas cards and plastic-coated playing cards are also available to be sold for the fund.

Another fund-raiser is used by some Auxiliaries at Christmas time. Physicians in the local society are asked to give up sending Christmas cards to one another and instead donate the money saved to AMA-ERF. They are urged to send a check in the amount they would ordinarily spend on Christmas cards to their Auxiliary. The money is tax deductible. The Auxiliary in turn sends a Christmas card, listing the name of all contributors to every medical society member and Auxiliary member. The cost of printing and mailing the card is underwritten by the Auxiliary and the funds sent to the National Auxiliary AMA-ERF fund.

## Voluntary Health Conference Scheduled

Changing relationships in the voluntary health movement will be the theme of a national invitational conference here February 16-17, 1966, sponsored by the American Medical Association Council on Voluntary Health Agencies.

Those invited include more than 300 representatives of the medical profession, national organizations, voluntary health and welfare agencies, business, labor, government, and education.

The conference will convene with a major address entitled, "Horizons in Communications and their Application to Public Attitudes," following a reception and dinner Wednesday evening, February 16. Four general sessions and two major addresses will follow on Thursday, February 17. The conference will adjourn at 4:30 p.m. that day. Registration will begin at 4 p.m. Wednesday, February 16, at the Continental Plaza Hotel.



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## OBITUARY

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### **Pinckney W. Snelling, M.D.**

**1897 - 1965**

Dr. Pinckney Welch Snelling died in Hyannis, Cape Cod, Massachusetts, October 30, 1965, after a long illness. He was 68 years of age. He leaves his wife Sarah Johnston Snelling, three daughters, a son, twelve grandchildren and three brothers.



Dr. Snelling was born in Athens, Georgia, March 15, 1897. He received his education in Georgia and Preparatory School of Woodbury Forest in Orange, Virginia. He graduated from the University of Georgia, 1917, and Harvard Medical School in 1921. He interned at the Hartford Hospital, and in 1923 entered Johns Hopkins Hospital for his residency in otolaryngology under Dr. Samuel Crow. In 1924 Johns Hopkins sent him to Germany to study ear pathology at Wurzburg, Germany. On his return he finished his residency in ear, nose, and throat specialty. Until his retirement to Cape Cod, Dr. Snelling was the Chief of the Department of Otolaryngology at the Hartford Hospital and consultant to several other hospitals in the Hartford area. He was a member of the Connecticut State Medical Society, the American Medical Association, a diplomate of the American Board of Otolaryngology, a member of the American Rhinologic Society, and the New England Otolaryngology Society.

Dr. Snelling was a keen and devoted physician and a meticulous surgeon, devoted to his patients and to the Hartford Hospital. He was an excellent administrator of the Department of Otolaryngology, and kept abreast of all progress in his specialty.

This spirit he infused into his entire staff. He arranged for two seminars of the American Rhinologic Society in Hartford which were attended by men from all over the country and was the recipient of the Golden Head Mirror award from the American Rhinologic Society. This was in recognition of his contributions to the furtherance of the science of rhinology.

We who served with him and under his direction benefited from his keen diagnostic mind and his enthusiasm for the progress of otolaryngology. Dr. Snelling's hobby was electronics and he was an amateur radio operator. Besides this, he was especially skilled with tools and had a complete workshop in his home.

MORRIS M. MANCOLL, M.D.  
and  
CHARLES A. TUCKER, M.D.

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## In Memoriam

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**Bodie, William J.**—Branford; Georgetown University School of Medicine, 1929. Dr. Bodie was a general practitioner in the Branford area for 34 years. He served in the Navy during World War I and in World War II was a major in the Army, serving as a transport surgeon. He received the Bronze Star medal and the U.S. Army Special Commendation medal for outstanding service. Dr. Bodie was a member of the American Medical Association, the Connecticut State Medical Society, and the New Haven County Medical Association. Dr. Bodie died December 21, at the age of 68.

**Keith, Albert R.**—Hartford; Harvard Medical School, 1903. Before retirement a few years ago, Dr. Keith was a surgeon and general practitioner in Hartford for more than 55 years. He was an honorary staff member of the Hartford Hospital. Dr. Keith was a member and past president of the Hartford Medical Society and the Hartford County Medical Association. He was also a member of the Connecticut State Medical Society, the American Medical Association, and the American College of Surgeons. He was a founder and past president of the New England Protologic Society and a member of the American Protologic Society. Dr. Keith died December 16, at the age of 90.

## Special Notices

### HARTFORD HOSPITAL SATURDAY MORNING 11 O'CLOCK GUEST SPEAKERS January 8 to March 26, 1966

- Jan. 8—*Lewis Dexter, M.D.*, Clin. Professor of Medicine, Harvard—Subject: "Pulmonary Embolism."
- Jan. 15—*James F. Patterson, M.D.*, Assoc. Professor of Medicine, Tufts—Subject: "Skin Lesions of G-I Disorders."
- Jan. 22—*David Seligson, M.D.*, Professor of Medicine and Pathology, Yale—Subject: "Chemical Instrumentation—Its Contribution to Patient Care."
- Jan. 29—*Harold N. Willard, M.D.*, Director of Chronic Care and Rehabilitation, The Thayer Hospital, Waterville, Maine—Subject: "The Challenge of Continuing Medical Care."
- Feb. 5—*Lawrence K. Pickett, M.D.*, Professor of Surgery and Pediatrics, Yale—Subject: "Surgical Aspects of Constipation in Children."
- Feb. 12—*George A. Wolf, Jr., M.D.*, Professor of Medicine, Tufts; Executive Director, New England Medical Center—Subject: "Does the Non-University Hospital Have Any thing to Offer in Medical Education?"
- Feb. 19—*Paul Dudley White, M.D.*, Clin. Professor of Medicine, Harvard—Subject: "The Long Follow-up: Cardiology in My Time."
- Feb. 26—*Frank B. Walsh, M.D.*, Professor of Ophthalmology, Johns Hopkins—Subject: "The Eye and the Central Nervous System."
- March 5—*Thomas C. Hall, M.D.*, Professor of Pathology, Harvard—Subject: "Recent Advances in Chemotherapy of Cancer."
- March 12—*Charles Eckert, M. D.*, Professor and Chairman, Department of Surgery, Albany—Subject: "Surgery of the Breast: Radical or Simple?"
- March 19—*Martin Stone, M.D.*, Profesof of Ob-Gyn, New York Medical College—Subject: 10:00 A.M.—"Intra-Uterine Devices"; 11:00 A.M.—"Family Planning."
- March 26—*Hartwell G. Thompson, Jr., M.D.*, Professor of Neurology, University of West Virginia Medical School—Subject: "The Enigma of Multiple Sclerosis."

### THE AMERICAN COLLEGE OF PHYSICIANS CANCER FOR THE INTERNIST

February 21-25, 1966

Presbyterian-St. Luke's Hospital  
1753 West Congress Parkway, Chicago, Illinois  
affiliated with

UNIVERSITY OF ILLINOIS COLLEGE OF MEDICINE  
Director

SAMUEL G. TAYLOR, III, M.D., F.A.C.P.

Fees: A.C.P. Members, \$60; Nonmembers, \$100  
Minimal Registration, 40; Maximal Registration, 125

Note: Registration forms and requests for information are to be directed to: Edward C. Rosenow, Jr., M.D., Executive Director, American College of Physicians, 4200 Pine Street, Philadelphia, Pennsylvania 19104.

### SUMMARY OF COURSE

The course will cover basic scientific and clinical aspects of cancer for the internist in the diagnosis and treatment of the cancer patient. It will include the mechanism of action of radiation and chemotherapy, and practical aspects of the biochemistry of growth. The role of the surgeon, the pathologist, the radiotherapist and the biochemist, together with the internist in the multiple disciplinary management of the cancer patient will be presented. Practical clinical chemotherapy for malignant disease offering worthwhile benefit will be adequately covered.

### HOTEL ACCOMMODATIONS

The La Salle Hotel, 10 North La Salle Street, Chicago, Illinois 60602. Mr. Don K. Miller, General Sales Manager. Single rooms, \$10.00 to \$18.00; twin-bedded rooms, \$16.00 to \$25.00.

When writing for reservations, please identify yourself with the College and with this particular course.

Note: Mrs. Samuel G. Taylor, III, will be glad to arrange entertainment for the wives of registrants, on a Dutch Treat basis.

### THE AMERICAN COLLEGE OF PHYSICIANS

Presents

Postgraduate Course No. 13

THE BIG HEART

March 7-11, 1966

BAYLOR UNIVERSITY COLLEGE OF MEDICINE

Meeting Place: Auditorium, Baylor University College of Medicine, Houston, Texas

Director: Raymond D. Pruitt, M.D., F.A.C.P.

Co-Directors: James K. Alexander, M.D., F.A.C.P.; G. William Curd, M.D., F.A.C.P.; Edward W. Dennis, M.D., F.A.C.P.

Fees: A.C.P. members, \$60; Nonmembers, \$100. Minimal Registration: 75; Maximal Registration: 125.

Note: Registration forms and requests for information are to be directed to: Edward C. Rosenow, Jr., M.D., Executive Director, American College of Physicians, 4200 Pine Street, Philadelphia, Pa. 19104.

Summary of Course: Four days of this five-day course will be devoted to discussion of problems related to cardiac hypertrophy. On the first day, consideration will be given to morphologic, physiologic, and biochemical aspects of cardiac hypertrophy. The second day will be devoted to discussion of clinical forms of cardiac hypertrophy, the third day to physical, roentgenographic and electrocardiographic considerations pertinent to the diagnosis of cardiac hypertrophy, and the final day to therapeutic problems, both surgical and medical, which derive from cardiac hypertrophy. The fifth day will be reserved for tours of the Texas Medical Center.

Hotel Accommodations: The Shamrock Hilton, Main at Holcombe Blvd., Houston, Texas, 77001. Mr. Gerald I. Jacobs, Sales Manager. Single rooms, \$8.00 to \$14.00; twin bedded rooms, 12.00 to \$18.00. When writing for reservations, please identify yourself with the College and with this particular course.



## **INSTITUTE FOR PHYSICIANS IN INDUSTRY**

**March 7-11, 1966**

The Program of Continuation Education of the Columbia University School of Public Health and Administrative Medicine announces the Ninth Annual Institute for Physicians in Industry. The one week course will be held at the Columbia-Presbyterian Medical Center complex in New York City during the week of March 7-11, 1966.

The institute is designed as an intensive refresher course relating to those subject areas of specific interest to physicians practicing in the field of occupational medicine. In addition, several sessions will be devoted to basic public health subjects. Physicians preparing to take specialty board examinations should find this institute particularly useful.

Further information and applications may be obtained from the Program of Continuation Education—Public Health, Suite 305, 21 Audubon Avenue, New York 32, New York. Telephone: (212) 568-4334.

## **5TH NATIONAL SYMPOSIUM SCHEDULED**

**March 10, 11, 1966**

The area of "Microcirculation" will be the topic of discussion at the Heart Association of Southeastern Pennsylvania's 5th National Symposium slated for Philadelphia's Sheraton Hotel, March 10 & 11, 1966.

Co-chairmen for this year's symposium are William L. Winters, Jr., M.D., associate professor of medicine at Temple University School of Medicine and Alfred N. Brest, M.D., assistant professor of medicine at Hahnemann Medical College and Hospital.

The symposium is part of the Heart Association's professional education program, designed to bring the latest available information from the research laboratories to the practicing physician.

Additional information may be obtained by contacting: Lyle L. Perry, Heart Association of Southeastern Penna., 318 S. 19th Street, Philadelphia, Pennsylvania 19103.

## **AMERICAN CANCER SOCIETY**

1966 Scientific Session

**May 11, 1966**

St. Francis Hotel, San Francisco, California

Sessions are open to all members of the Medical and Dental Professions and Students. No advance registration or registration fee.

## **Announcement Of A Special Symposium At Yale University School Of Medicine January 18, 1966**

**"FAMILY MEDICAL CARE IN AN AGE  
OF SPECIALIZATION"**

Moderator: Dr. E. Richard Weinerman (New Haven)

Participants: Dr. Frederick C. Gevalt, Jr. (Sharon), Dr. John C. Leonard (Hartford), Dr. Waldo E. Martin (Milford), Dr. Bruce R. Valentine (Abington).

a panel discussion to be held on  
Tuesday, January 18, 1966 at 4:30 P.M.  
Mary S. Harkness Memorial Auditorium  
Yale University School of Medicine  
333 Cedar Street, New Haven

## **New Volume On Cutaneous Toxicity**

"Cutaneous Toxicity," symposium by American Medical Association and Society of Toxicology, October 1965, clothbound, \$8; paperbound, \$6.

The effects of new chemicals on the human skin is the subject of a new volume to be published by the American Medical Association in cooperation with the Society of Toxicology.

"Cutaneous Toxicity" contains papers presented at a recent symposium sponsored by the two groups, and concerned with problems resulting from chemical contact with human skin.

Contributors to the symposium are experts from many scientific disciplines. Much of the information they presented has not been generally available until publication of this volume. The foreword is by Harry W. Hays of the Advisory Center on Toxicology, the National Academy of Sciences, and National Research Council.

The book will be of special value to those interested in the physiology of the skin and cutaneous health. Topics include the nature of the epidermal barrier, the adequacy of existing skin treatment techniques, and the problem of relating animal research data to man.

The volume will appear as a supplement to Toxicology and Applied Pharmacology, official journal of the Society of Toxicology.

Copies are available at \$6, paperbound, or \$8, clothbound, from Academic Press Inc., 111 Fifth Avenue, New York, New York 10003.

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## **Doctor's Office**

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Dr. Richard M. Campbell-Jacobs announces the opening of an office for the practice of general orthopedic surgery at 45 Crescent Street, Middletown.

Dr. John H. Foster, announces the removal of his office for the practice of internal medicine to 163 Grove Street, Waterbury.

Dr. Kenneth R. Kaess, D.A.B.R. and Associates, announce the opening of their office for the practice of radiology and nuclear medicine at 1132 Meriden Road, Waterbury.

Dr. Thomas A. O'Boyle, announces the opening of an office for the practice of pediatrics at 57 Union Street, Rockville.

Dr. Joseph P. Shea and Dr. Robert W. Berry, announce their association with Dr. S. E. Marrash in the practice of thoracic and cardiovascular surgery at 2660 Main Street, Bridgeport

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## NEW BOOKS IN REVIEW

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**APPLIED HYPNOSIS AND POSITIVE SUGGESTION.** *In Medicine, Dentistry and Patient Care.* George A. Ulett, M.D. and Donald B. Peterson, Editors, The C.V. Mosby Co., St. Louis, Missouri, 1965, 134 pp., \$8.50.

Reviewed by: LOUIS H. NAHUM

There are many books available on the subject of hypnosis. This book looks upon it as a useful extension of doctor-patient relationship. It is a means by which statements, suggestions, and "the doctor's orders" are conveyed to the patient so that a variety of procedures and treatment are facilitated.

Hypnotizability the authors emphasize—the ability to accept uncritically and act upon a verbal or non-verbal suggestion—is an intrinsic characteristic of the human mind present in the individual to a variable degree and operating more or less all the time. Because of these features, hypnosis can be highly important in the practice of medicine. Nevertheless, it is generally ignored in the curricula of most medical schools.

This volume throws sharp light on the implications this subject has, in the practice of medicine, dentistry and patient care. An understanding of this technique by the nurse, surgeon, anesthetist, general practitioner, psychiatrist, or other members of the healing art team will make hypnosis truly adjunctive.

The book in its few short pages, consisting of 15 chapters is, lucid, clearly written and really a revelation to members of the healing art. In the introduction the groundwork of the purpose of hypnosis is laid. There is then a scholarly compilation of important names in the history. There follow nature of hypnosis, theories, induction, techniques, and speech as an instrument of hypnosis, and positive suggestion we all can use and do, in the care of patients.

There follows chapters on autohypnosis, hypnosis in surgery, anesthesia, and analgesia, in dentistry, in obstetrics, in psychiatry, in habit control and in children. In the concluding chapters we find discussion of placebos, amnesia, convulsive disorders, malingering and conclusions. There is a good bibliography and useful suggested references.

It is clear from the topics discussed that the authors have excellently illustrated the wide application of this subject and its pertinence to many different kinds of medical and even social questions. The authors have succeeded fully in this purpose to stimulate the reader to try hypnotic techniques as an aid in solving some of the problems met in our daily practice of the healing art. It should be emphasized however that the technique must be learned thoroughly before its trial on patients just as a gastrectomy cannot be tried without thorough preparation and development of skill.

**THE THYROID GLAND, Volume 1, Volume 2, Edited by Rosalind Pitt-Rivers and W. R. Trotter, Volume 1, 154 pp., Volume 2, 336 pp., Butterworth, Inc., Washington, D. C., 20014, 1964, \$29.50 set.**

Reviewed by: ALVIN BRODISH

The specific purpose of this two-volume set is to provide an authoritative, up-to-date and convenient reference which summarizes current knowledge of the thyroid gland. Volume 1 is primarily concerned with the structure and function of the normal gland, derived for the most part from animal experimentation. Volume 2 deals with naturally-occurring human disease with observations based largely on clinical observation and investigation.

Volume 1 contains complete and authoritative information on the morphology, embryology, biochemistry and physiology of the normal thyroid gland. Some of the topics included in this volume are: development of the human thyroid gland, morphology and cytology, iodide metabolism and thyroid hormone biosynthesis, distribution and metabolism of thyroid hormones, physiological activity and mechanism of action of thyroid hormones and analogues, antithyroid compounds, and finally, applications of radioactive isotopes of iodine.

The chapters are written by workers who have themselves made distinguished contributions to the field and most of the contributors are currently engaged in thyroid research or in the treatment of thyroid disease. Therefore the contents are up-to-date and as a result of minimal editorial restraint the authors have been left free to interpret and express their ideas in their own style. In general the text is well-written and adequately illustrated. The chapter on morphology and cytology contains particularly excellent photographs of the histology and fine structure of the thyroid.

Volume 2 deals with the cause and effect of deranged thyroid physiology in human thyroid disease. The opening chapter by H. D. Purves is a particularly good summary of knowledge of the control of thyroid function in which he raises some stimulating and provocative points regarding current concepts of the regulation of thyroid function. Other chapters discuss iodine metabolism in thyroid dysfunction, various types of goiter, hypothyroidism, thyroiditis, hyperthyroidism, thyroid cancer, and other clinical syndromes associated with thyroid disease.

Together, these two volumes provide a wealth of information, conveniently summarized, on the current knowledge of the thyroid gland. The comprehensive bibliography at the end of each chapter makes this set a valuable reference source for those involved with current research on the thyroid gland, or with the treatment of thyroid disease.





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This, mind you, is no skimpy group certificate—but an individual policy with guaranteed rates—dividend

provisions—and an extremely liberal waiver of premium clause.

Obviously this space is too small to attempt to adequately describe the plan, especially since we have gone to no small expense to prepare a brochure for you **just** for this purpose.

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**CIBA Foundation Symposium: COMPLEMENT, ed.: G. E. W. Wolstenholme and Julie Knight. Little, Brown and Co., Boston, 1965, 388 pp. with 50 illustrations, \$12.50.**

Reviewed by: JOSEPH R. BOYLE

This volume is the proceedings of a Symposium on Complement held in May of 1964. At that time twenty-five of the world's experts on the subject reviewed their own recent work and openly discussed all aspects of complement. The book gives each formal presentation as well as the discussion which followed. Subjects range from Mechanism of Hemolysis By Complement (M. M. Mayer) to the Possible Role of Complement in Autoaggressive Processes (H. J. Müller-Eberhard). Many of the titles have clinical appeal but the subject matter presented is more suitable for those with a research interest in complement and its relation to basic biologic phenomena. The presentations and discussions are geared to a highly specialized group of scientists and for them the volume is excellent.

Mayer reviews the reactions between complement and sensitized antigenic sites that eventually lead to the hemolytic lesion in the red cell membrane. He suggests that one effective "hit" by complement is sufficient for lysis. He defines complement in terms of a cytotoxic reaction system activated by antigen-antibody complexes—but others take exception to this. The roles of complement in bacterial reactions (L. H. Muschel), phagocytosis (S. V. Boyden), immune adherence (D. S. Nelson), hemolysis *in vivo* (P. L. Mollison) and paroxysmal nocturnal hemoglobinuria (J. V. Dacie) are covered.

The book is recommended for those with a background and special interest in complement. Others beware!

**MANAGEMENT OF THE PATIENT WITH CANCER. Edited by Thomas F. Nealon, Jr., M.D., with contributions by seventy-one authorities. W. B. Saunders Company, Philadelphia, 1965. 1067 pp. Illustrated. \$27.50.**

Reviewed by: IRA S. GOLDENBERG

A marked difference of opinion exists among physicians as to whether cancer should be treated as a single disease entity involving multiple body systems or whether it should be considered as simply a disease which may involve one or another anatomical subdivision. This divergence of thought leads to texts devoted exclusively to cancer versus those in which cancer management is discussed in chapters under the separate anatomical specialties. This book, edited by Dr. Nealon, who is Professor of Surgery at Jefferson Medical College, belongs in the former category and the subject is well handled by an outstanding group of 71 authors.

General considerations of cancer including discussions of pathology, radiological diagnosis, cytology, and therapy with surgery, radiation and chemotherapeutic agents precede specific detailed anatomic site presentations of all aspects of the disease in each organ. It is refreshing to read the words of many physicians who previously have not published extensively on these topics.

This is a practical book for the physician who treats patients. Succinct composition of the text takes the reader through all aspects of each problem with a minimum of

verbosity and a good index makes the material easily available. This volume provides information on the accepted approach today to cancer in its myriad forms and what treatment results can be expected. W. B. Saunders Company has done its usual excellent job of typography, reproduction of illustrations and binding. Although costly, I recommend this book for the library of any physician who manages patients with cancer.

**A LITTLE STORK TOLD ME. Author: Kenneth R. Morgan, M.D. William Morrow & Company, New York, 1965. 128 pp. \$2.95.**

Reviewed by: ORVAN W. HESS

This 128 page treatise, described as a "cautionary guide for expectant parents," was written by a Connecticut obstetrician and gynecologist. The author has used the literary forms of humor and satire as effective means of communication. In this book, based on his experiences in practice and a point of view tempered by broad insight not restricted to the purely scientific, he presents an explanation for many of the common problems and reactions of parents-to-be. Directed, as it is, to those who make up a large segment of society, this book should be widely read.

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## BOOKS RECEIVED

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*Books received for review are acknowledged in this department and such acknowledgement must be regarded as a sufficient return for the courtesy of the sender. Selection will be made for review in the interests of our readers and as space permits.*

*The Body.* By Alan E. Nourse and The Editors of Life. Sixth volume in the Life Science Library series. Previously published: *Mathematics, Matter, Energy, Machines, The Cell.* Published by Time Inc., New York. 200 pp. Illustrated (72 pp. in full color). Price \$3.95. Available on order from Time Inc., Book Division, 540 North Michigan Avenue, Chicago, Illinois.

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*The Burn Wound.* Captain Stanley E. Order, M.D. and Colonel John A. Moncrief, M.D. The Charles C. Thomas Company, Springfield, Illinois, 1965. 72 pp. Illustrated. \$7.75.

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*Advances In Oxytocin Research.* Edited by J. H. M. Pinkerton. Proceedings of a Symposium held on 1st May 1964 under auspices of the Blair-Bell Research Society. Symposium Publications Division, Pergamon Press, New York, N. Y. 150 pp. \$10.00.

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*Atlas of Pulpal And Peripical Biology.* By Alfred L. Ogilvie and John I. Ingle. Lea & Febiger, Philadelphia, Pennsylvania. 1965. 169 pp. 199 illustrations on 149 figures. \$5.00.



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## MEDICAL NEWS

### Recovering From "Heart Attacks"

Frightened and depressed after suffering an acute "heart attack," a patient sometimes is convinced he is sicker than he really is.

The result may be lingering invalidism which works a hardship on both the patient and his family, points out an article in the current *Journal of the American Medical Association*.

Staff members at Duke University School of Medicine examined 20 men who were making slow progress in recuperating from acute myocardial infarction (coronary artery obstruction). They found:

1. Widespread belief among patients and their families that the heart remains "very fragile" after an attack. There was great fear of physical activity.

2. Depression and frequent chest pains in the men, although these pains were not related to the attack.

3. Overprotectiveness by some patients' wives. Even when some men made an effort to return to normal activities, their wives wouldn't let them. On the other hand, some men were overcautious themselves.

The authors of the article are Robert F. Klein, M.D., Alfred Dean, Ph.D., L. Montgomery Willson, and Morton D. Bogdonoff, M.D.

The sample of 20 patients cannot be considered representative of all cases of myocardial infarction, the authors point out, but these patients represent characteristics that many physicians have observed.

Fear and depression are "legitimate and important responses" to serious heart disease, said a *Journal* editorial. However, certain features of emotional invalidism begin early in convalescence. The physician has to be on guard against these, the editorial said.

The authors of the article suggest several remedies. Physicians should clearly explain the multiple types of chest pain likely to follow a myocardial infarction, they said. Doctors also should later modify the strict instructions, given immediately after an attack, for the patient to "take it easy."

A patient's anxiety, fear, or depression, should be explained to him as being legitimate and important, the authors said.

The patient's spouse should be included in the discussions, they said. The doctor "should be par-

ticularly alert to anxiety-engendered overprotectiveness in the spouse." There should be a gradual step-up of the patient's activity.

Of the 20 men studied, 12 had never returned to work following their first myocardial infarction. Only three returned to full-time work at their former jobs. Two others were at work full-time in new jobs, and three did part-time work. The mean time since their first attacks was 22 months.

Recurring chest pain was reported by 12 of the men; 17 noted fatigue, and 14 complained of shortness of breath. Troubled sleeping was reported by 14 patients, and nervousness was acknowledged by 17.

In every case, however, the observers felt that the patients had made a slower-than-necessary recovery.

"The patient with a history of myocardial infarction often considers himself, or is considered by others, to be 'the man on a tightrope'," said the *Journal* editorial. "The fear of sudden death and the fear of activity resulting from this conception are neglected but crucial phenomena in our society. The suggestions . . . presented by these investigators can do much to decrease the incidence of post-myocardial infarction invalidism."

### Today's Health Guide A Best-Seller

More than 80,000 volumes of *Today's Health Guide* have been sold since the American Medical Association's new family health manual went on sale recently.

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*Today's Health Guide* is the product of the combined knowledge and experience of many doctors and allied scientists. It is the AMA's latest effort to help American families make best use of their health resources.

*This Week* magazine called the 624-page guide "a book which is sure to rank among the most remarkable medical works of our time." *This Week* devoted an entire issue to excerpts from the book.

*Today's Health Guide* is available at the special price of \$4.95. Send check or money order to the American Medical Association, 535 N. Dearborn Street, Chicago, Illinois 60610.





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### **Contraindications**

Pregnancy; disease of the central nervous system; evidence or history of blood dyscrasia.

### **Precautions and Side Effects**

Complete blood cell counts should be made before and after therapy, especially if a second course is necessary.

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## **Nutrition Problems Considered By AMA**

Hunger haunts a large part of the world, and the problems it causes are growing, day by day.

Even in the United States, where food is in superabundance, there is a certain amount of malnutrition, largely caused by ignorance and poverty.

On the other hand, many Americans eat too much for their own good. Still others have health problems which limit the kinds of food they can eat. In short, every American family is concerned about nutrition. It's a vital factor in personal health.

In larger terms, however, the improvement of nutrition is a pressing need for the welfare of the world.

The current issue of Today's Health magazine, published by the American Medical Association, is devoted to food and nutrition. Articles describe the serious nutrition problems of Latin America, how better nutrition is made possible through research and education, and how millions of Americans are duped every year by the claims of "health food" faddists.

Other Today's Health articles describe how veterinarians safeguard this nation's meat supply, and how those on a gluten-free diet can enjoy tasty meats. Protein, the workhorse of the nutrient

family, is described in an article by Donald G. Cooley. Daily protein goals are illustrated for each member of the family.

In the United States, nutrition education and research has been supported since 1941 by the Nutrition Foundation, a non-profit organization founded by leaders in the food and allied industries. A Today's Health article tells how the Foundation is using educational programs to promote a greater understanding of nutritional values, both in this country and in Latin America. Scientists supported by the organization have had remarkable success in discovering some of the basic information about nutrition.

The special issue of Today's Health precedes a Western Hemisphere Nutrition Congress to be sponsored by the AMA Council on Foods and Nutrition, November 8-11 in Chicago.

The full range of Western Hemisphere nutrition problems will be considered at the Congress, from food regulations to infant feeding, from food-borne diseases to new discoveries in nutrition. More than 60 speakers from South America, North America, Europe and Africa will present papers.

Now is an excellent time to concentrate on the world's nutrition problems, particularly those of the Western Hemisphere, said Philip L. White, Sc.D., director of the AMA Department of Foods

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and Nutrition. Dr. White also is secretary to the AMA Council on Foods and Nutrition.

Food deficiencies in Latin America can't be corrected by dole-type surplus food programs, Dr. White said. Protein, vitamin and other nutritional deficiencies may come about through a complex combination of factors: underproduction of food, maldistribution of food, or failure of parents to understand or use good nutritional practices.

A prominent feature of the nutrition congress will be its interdisciplinary approach to food problems. Correction of malnutrition and undernutrition in a nation, said Dr. White, must come through such measures as improving food industries, improving agricultural technology, upgrading food processing and food storage to cut losses, and educating the populace in health, nutrition and home economics.

The special issue of Today's Health magazine, of wide interest to the public, and later, the Western Hemisphere Nutrition Congress, of interest to many types of scientists, are part of the AMA's continuing efforts to promote good health. Copies of Today's Health are available now on newsstands or by subscription (\$4 a year, U.S. and Canada; \$6 elsewhere) from the American Medical Association, 535 N. Dearborn St., Chicago, Ill. 60610.

## Hypnosis

Hypnosis is not a toy and unwise use may seriously affect an individual's physical and emotional health, says a pamphlet of the American Medical Association.

About one person in four can be deeply hypnotized in a relatively short period of time and most people can be hypnotized to some degree. No one is sure why some people can be hypnotized and others not.

Hypnosis can be easily taught in half an hour and can be self-taught from a book. No equipment is needed other than the voice of the hypnotist.

*But hypnosis is dangerous in the hands of an amateur and should be used only by qualified professionals.*

The most common medical use of hypnosis is as an anesthetic. Patients have been hypnotized for childbirth, for dental surgery, during the setting of a fracture and for other forms of surgery. It has also been used to ease anxiety and in the management of painful symptoms such as headache. Obese patients have lost weight as a result of hypnotic suggestion and smokers have been able to cut down or quit entirely.

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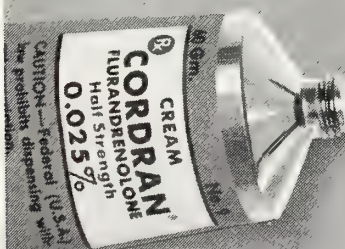
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PRIMITIVE MEDICINE (see page 85)

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# Connecticut Medicine

## editorials

### Ability Lost vs Ability Retained

The physician is frequently called upon to evaluate objectively the degree of physical impairment which a given patient has sustained either from naturally occurring disease or from accident. The purpose of such an evaluation is to determine whether the functional loss is sufficient to prevent the individual from returning to the work which he has done before. Obviously each discipline has its own objective functional tests, the evaluation of which can lead the physician to estimate disability. Lundgren, Müller and Gaenster have just published very revealing information on pulmonary impairment and disability claims. One hundred persons claiming total and permanent disability because of pulmonary disease or dyspnoea were compared with one hundred patients without disability claims who had similar age and sex distribution and virtually identical lung function profiles.

The remarkable facts emerged from the comparison of the claimants and non-claimants for permanent total disability. One was that among the claimants 46 per cent had no discernible pulmonary impairment. Their main problems were inactive tuberculosis, insignificant heart disease, psychiatric problems, obesity and alcoholism. Although initially Lindgren thought that these 46 per cent might have serious impairment of other organ systems, this was found not to be the case.

The largest single number, 18 patients, had old inactive tuberculosis. Several with old minimal disease had never worked after this initial illness and gave the history of tuberculosis as the sole reason for disability or inability to find employment. This

problem of tuberculosis is especially worth considering. There was a history of this disease in 31 claimants, yet 18 had no measurable impairment and 13 others had only moderate impairment. Most patients had minimal or moderately advanced disease classified as "inactive" for more than three years. Several had not worked for many years and ascribed this simply to the fact that had tuberculosis (!) or to their physician's advice at one time, against exertion. These individuals illustrate the detrimental effects upon some individuals of prolonged sanatorium care with the emphasis in the past on bed rest and inactivity.

There were 10 claimants with questionable or definite heart disease, but apparently not sufficient to prevent some activity. An obvious cause of dyspnoea in the absence of significant pulmonary impairment was obesity. Alcohol was sometimes the sole problem and contributed to unemployment in eight of the 18 patients with a history of tuberculosis.

By contrast 88 of the control group who were fully active and gainfully employed did not differ significantly from the claimants in several of the ventilatory tests used for each group, to determine their ventilatory capacity. It is revealing that the capacity of the control group showed an average reduction to about  $\frac{2}{3}$  normal. For a given relationship between ventilatory demand and ventilatory capacity, the claimants had more subjective complaints and their judgment of dyspnoea was not as good as it was among the control patients. It seems as if the claimants for disability concentrated upon the degree of ability they had lost, whereas the control group concentrated upon the degree of ability

## THE COVER

### PRIMITIVE MEDICINE

PRIMITIVE medicine is timeless. It is as old as the cave dweller, yet in many remote parts of the world its practice is as new as today. The sand-painting ceremonies of American Navaho Indians are unusually beautiful examples of primitive medicine, embodying all its elements—physio—and psychotherapy, religion, magic, singing, and drug lore. In a medicine "hogan," family and friends join in the Mountain Chant's nine-day ceremonies, in which this sand painting has an important part. The "singer" (medicine man) sings, prays, and manipulates magico-religious artifacts. Herb preparations given the patient are shared by the "singer" and the spectators too in this primitive rite.

they had retained. In short, there was a wide discrepancy between the claimants and the control group that can only be explained by psychological and socio-economic factors.

A complaint of shortness of breath is a good example of the psychological factors involved in claiming disability. To speak of shortness of breath, it must be recognized as being preceded by a series of events. First, the patient must become aware that his breathing requires a conscious and perhaps difficult effort. Next he must judge whether this difficulty is normal for his age, training and degree of exertion. Finally, he must communicate the nature of the sensation to his physician. All these factors make for wide variation in patients' complaints who have equal degrees of pulmonary impairment. Some claimants for total disability complained of dyspnoea even though they had better lung function than those in the control group who were gainfully employed. Actually on closer questioning some of the claimant group with complaint of "shortness of breath" proved to have an altogether different symptom such as angina pectoris, dizziness and back pain! In short, these people confused disability and medical impairment.

These two terms are often confused. Impairment is a purely medical condition which the physician alone is competent to evaluate. On the other hand, disability is a more complex condition and its evaluation involves more than just a medical judgment. For there is involved an appraisal of the patient's ability to engage in gainful activity which is affected by many factors such as the individual's nature, intelligence, education, economic and social environment, the local labor market, employer's prejudices as to age, sex, race. Then there is the insurance company's attitude towards coverage of the handicapped, laws concerning waivers and many more.

As it turned out in Lindgren's study, these socio-economic factors may be decisive in many situations and medical impairment is just one important contributing factor, but not necessarily the sole indication of the extent of the patient's disability. The truth is that there is a difference between the degree of impairment and the degree of residual function. If we think of disability in terms of the patient's lack of ability to earn wages, then this may not be related at all to degree of diminution of maximum capacity. A man may retain sufficient physiologic capacity to earn a wage and this capacity may be a small part of the capacity of a hypothetically normal man. He may however still be unable to be gainfully employed for other reasons.

Many individuals with moderate impairment can do any kind of work except "heavy manual labor."

Presumably reference is made to work requiring perhaps a ten-fold increase in energy expenditure. The review of the occupations the claimants for total disability who were classified as laborers "doing heavy work" suggests that at least in this area, occupations requiring such "heavy manual labor" have largely disappeared. Cooks, dishwashers, custodians and elevator operators are never called upon to increase greatly their oxygen consumption. Even construction laborers, longshoremen and coal miners have become part of a mechanized team.

Actually in many instances the greatest physical exertion of daily living are those of travel to and from work under adverse circumstances and of recreational activities. This is borne out in Lindgren's study which shows that over 10 per cent of the control patients were gainfully employed with a maximum breathing capacity of less than 40 liters per minute. Instead of thinking as one usually does in terms of loss of ability, it is important rather to think in terms of the amount of ability that is retained. If this point of view is followed, it will be found that incapacity in many instances is really not due to physical impairment alone.

Because of the complexity of the problem of determining disability as distinct from physical impairment, the physician is understandably reluctant to decide upon disability when his chief task has been to determine degree of functional impairment.

L.H.N.

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### Electrocardiographic Monitoring Of Post-Myocardial Infarction

The physician is still in need of a reliable method to determine how much activity he can safely prescribe to a patient recovering from acute myocardial infarction. Cain et al<sup>1</sup> have recently proposed the routine use of electrocardiographic monitoring of activity in the management of such patients. It is based upon the well recognized fact that the electrocardiogram in its ST segment and T wave configuration can reveal the presence of myocardial ischemia. A patient recovering from myocardial infarction, just like one who suffers from angina pectoris, when he exceeds his capacity, will show classical changes in the electrocardiogram of the ST and T wave as well as ventricular ectopia. Such an objective sign is unmistakable evidence that the patient must do less than will produce such changes. The authors have specified ten successive daily activity levels following which the patients were



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tested electrocardiographically. Activity level 1-3 consists of mild exercise in or close to the bed. Activity levels 4-6 consist of increasing distances of level walking and activity levels 7-10 consist of inclined plane walking, or light handiwork in the occupational therapy clinic and finally climbing one flight of stairs.

Electrocardiograms were made routinely for activity levels 1, 4, 7 and 10 and repeated at any activity level if physical or electrocardiographic abnormalities were detected. If the electrocardiogram demonstrated significant changes after activity, the patient was restricted for one week to less stressing activity levels which he has already performed safely, before he was retested. A minimum of fifteen minutes of bed rest preceded the pre-activity control tracing and a second tracing was taken immediately after activity. Fortunately, the authors in treating 335 patients over a period of two years found that a single standard precordial lead is adequate to detect myocardial ischemia or ventricular arrhythmia. This made testing easy and rapid.

The authors were careful in their interpretation of a positive test. An ST segment shift of 1.0 mm or more was considered to indicate the presence of coronary insufficiency. A T wave lowering usually accompanied the ST segment shift and contributed to the interpretation of greater pathologic significance. On the other hand merely a junctional depression while it could have pathologic implications was not necessarily synonymous with ST segment deviations and could have been the result of overactivity of the sympathetic nervous system. Neither did they attribute much importance to T changes alone since T wave rise without ST segment shift occurred frequently and inverted T waves occasionally returned to a normal configuration after exercise. It is hoped that the prognostic significance of this finding will be explored by the authors in a future communication.

Patients were not tested during the first fifteen days after acute myocardial infarction. Most of the patients started their program between the 18th and the 30th day after the acute episode and had previously been restricted to bed, chair and commode. Although earliest post-myocardial infarction performance with an abnormal electrocardiogram was obtained on the 15th and 19th day, in all other instances abnormal electrocardiograms were obtained for periods later than the 25th day after infarction. In all the patients tested only one had angina and a remarkable degree of dyspnea and fatigue.

It is clear that electrocardiographic monitoring provides evidence to indicate if the tested levels of stress are safely tolerated by the patient with recent

myocardial infarction. This gives the physician a reliable method to determine how much activity he can safely prescribe. The patient is psychologically reassured as he is guided through the program by his physician. At the same time the patient is trained to observe his activities relative to his energy cost.

About half of the patients negotiated their ten activity levels of the program without difficulty. Eighty-two passed the total program after periods of delay. At the end all demonstrated ability to climb stairs safely. The net effect of the program therefore was to permit the physician to safely prescribe more demanding activity and at an earlier period of convalescence than is habitual. What is important is that the presence of severe coronary insufficiency is usually discovered during the first three activity levels, that activity tolerance is likely to keep improving gradually up to two years after infarction and that the way patients respond to activity levels offers information of prognostic significance in terms of longevity and ultimate capacity for rehabilitation of the cardiac.

Every good physician uses pulse, blood pressure, dyspnea, fatigue and pain to guide him in rehabilitating the patient recovering from myocardial infarction. But quantitation and objective criteria is the ultimate aim in evaluation of any therapy. This Cain et al have further helped the physician to attain in rehabilitating the patient recovering from acute myocardial infarction.

L.H.N.

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## Potential Of Anticoagulants By Other Administered Drugs

The course of maintaining therapeutic levels of the prothrombin time during prolonged anticoagulation therapy does not always run smoothly. Not infrequently we find a patient with a prothrombin time of 30 seconds one month and 18 seconds the next month. This exasperating occurrence arouses our suspicion that one of several causes must be entertained. Our first thought is that the patient may not have followed his instructions consistently. This is rarely the cause. Another is that perhaps the laboratory estimation of the prothrombin time may be at fault. In the numerous instances that an unacceptable figure has been reported, a repeat check by the laboratory has confirmed the

accuracy of the test. Many times we have speculated that perhaps the anticoagulant has not been absorbed or that certain products of bacterial metabolism in the bowel are absorbed to antagonize the systemic action of the anticoagulant. Such speculations are not helpful in solving the problem.

Carter<sup>1</sup> has just brought to our attention another factor: potentiation of the effect of orally administered anticoagulants by other administered drugs, in his case phenylramidol. It has been well known that in principle administration of one drug may inhibit or potentiate the effects of another.<sup>2</sup> Such an interaction is of particular clinical importance when anticoagulants are given, because its recognition may prevent serious hemorrhagic complications and may result in a smoother control of the prothrombin time.

Carter's report deals with the effect of phenylramidol hydrochloride (analexin) on the response to orally administered anticoagulants. This drug is marketed for use in acute and chronic conditions in which muscle spasm and pain are involved. It is reported to have an analgesic and some muscle relaxant activity.<sup>3,4</sup> When given by itself for periods up to 22 weeks, only 4 percent showed gastric irritation, drowsiness, pruritis and rash. Since the drug is used relatively frequently it is surprising that no previous reports on its potentiation of anticoagulant drugs has been reported.

The possibility that the drug would potentiate the effects of anticoagulants was first considered when two of Carter's patients on long term anticoagulant therapy showed marked prolongation of the prothrombin time after they were given phenylramidol for back pain. In one of the patients generalized hemorrhagic manifestations developed. Carter was not satisfied to treat this observation in passing but with aroused curiosity he wondered whether the phenylramidol truly potentiated the anticoagulant. Accordingly he collected 11 patients on anticoagulants who were also taking the muscle relaxant drug and compared them with 10 others not on anticoagulants. The patients taking both anticoagulants and phenylramidol showed a rapid increase in their prothrombin time, while the patients only on phenylramidol retained a normal prothrombin time.

It is well to remember that there are already several drugs known to influence the effect of orally administered anticoagulants on the prothrombin time. Those that inhibit it include Vitamin K and phenobarbital (2.6). On the other hand, salicylates, sulphonamide, bowel sterilizing antibiotics, phenylbutazone and now pyramidol increase the effect of anticoagulants.

When considering what the mechanism might be by means of which these potentiating drugs act, one

is in purely speculative territory. Burns<sup>2</sup> recently called attention to enzyme induction as an important mechanism in drug interaction. It appears that many drugs stimulate or inhibit enzymes that are concerned with their own metabolism or with the metabolism of other drugs thereby either diminishing or increasing the drug effect. Burns thinks that phenobarbital reduces action of anticoagulants and phenylbutazone increases their action in some such manner. It is of course possible that phenylramidol also potentiates the effect of anticoagulants by some such mechanism. It can be imagined that its influence could be exerted by preventing removal of the anticoagulant at its specific site of action or more remotely by interfering with the excretion of the anticoagulant from the body. These speculations merely mean that much more biochemical studies are required to elucidate the mechanism of potentiation.

It is likely that the list of drugs that affect the action of anticoagulants will continue to grow.<sup>7,8</sup> This of course will increase the already difficult task of controlling the prothrombin time in patients on anticoagulant therapy, since we know most patients receive several medications at one time.

This means that physicians who supervise long-term anticoagulant therapy must be thoroughly familiar with the drugs that affect the action of anticoagulants and they should operate always with a high index of suspicion regarding other drugs that might yet be discovered to have such an effect. Starting a patient who is already on long-term anticoagulant therapy, on a new drug may be particularly hazardous when the patient is under the care of more than one physician, a situation frequently present in hospitals, out-patient departments and in group clinics.

However, even when such a patient is under the care of one physician, the recognition that some drugs interfere with the action of anticoagulants like phenobarbital while others potentiate such action can make understandable many perplexing problems we have all faced in maintaining smooth control of prothrombin time by anticoagulants taken over long periods of time.

L.H.N.

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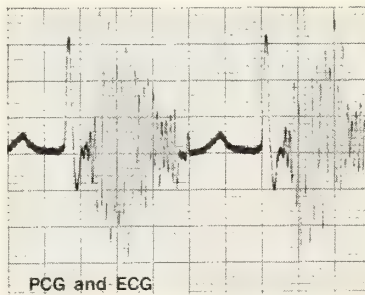
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\*\* Denotes resolution of at least 50%.

\* Denotes resolution up to 50%.

### DURATION OF TREATMENT

| Number of Cases             | 14     | 24    | 18     | 14     | 9      | 3      | 7      | 4      |
|-----------------------------|--------|-------|--------|--------|--------|--------|--------|--------|
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## Whither Goest The Autopsy

In 1793 Baillie wrote "it is very much to be regretted that the knowledge of morbid structure does not lead with certainty to the knowledge of morbid actions, although the one is the effect of the other; Yet surely it lays the most solid foundation for prosecuting such inquiries with success." This is as true today as it was then, except that the prosecution of the knowledge of morbid actions and their causes has become increasingly insistent as new techniques for their study have recently become available.

A glimpse merely at the problem of virus diseases makes clear the great complexity of solving some problems at the autopsy table. Isolation of viruses from tissues of the heart, lung, liver and other organs, invaded by the numerous separate viruses, now require maintenance of a variety of cell lines in tissue culture; a large group of laboratory animals of differing susceptibilities. Then electron microscopy, histochemistry and in some cytochemistry, physical and immunological methods at times need to be extended to the autopsy.

Such probing autopsy studies require collaboration of several departments and use of specialized skills, expensive equipment and personnel. It is obvious why the usual autopsy performed at small hospitals where such skills are not available and even in large centers, is coming under careful scrutiny as to its potential for revealing new truths that will advance knowledge in the handling of the sick by the clinician.<sup>1-6</sup> In spite of the fact that there has been much lip-service directed only to securing the required percentage of postmortems for official approval of a hospital, the fact remains that in a number of instances the clinician already has made a diagnosis from the assistance he receives from laboratory and other techniques, often expects little more from the necropsy and frequently does not even feel the necessity to bring to the pathologist the clinical problems he encountered and collaborate with him in seeking an answer at the autopsy table.

Throughout the development of medical science the autopsy has afforded a major means for the recognition of new disease, for the establishment of pathogenesis and for the evaluation of the effects or effectiveness of new therapy. It has served as the basis for developing accuracy in clinical diagnosis and led to the establishment of most disease entities as we know them. It is not surprising therefore that before the present era, great clinicians like Osler and Blumer went to the clinic from the autopsy table.

Because of the great advances in clinical methods and the use of medical laboratory information acquired from the living, the autopsy has to a much less degree provided any unique service for evaluation and has demanded less interest on the part of the clinicians. Frequently the cause of death may appear obvious and except in unusual cases requires necropsy, evaluation mainly for medico-legal reasons, and then by a forensic pathologist. A lack of interest in autopsies which have become unnecessarily repetitious is quite understandable. Many diseases such as proved cancer with extensive metastases have become regarded by both pathologists and clinicians merely as an arduous exercise and are of little significance for clinical correlation. They present no new scientific information and are repetitious, offering no contribution to the clinical evaluation of symptoms and therapy of the disease, in short, without educational value either to the pathologist or the clinician.

It seems reasonable now that autopsies have risen five times in cost, that pathologists should devote less time to performing autopsies of questionable clinical, research and educational value and allow more time for full and efficient study in those instances where a productive effect would be achieved. In short, we have reached a point where performing an autopsy should not be an automatic event and we should think more about the matter of selection. Hazard<sup>1</sup> believed that we should seek to perform autopsies in three special areas. One is in those instances that benefit the care of future patients through scientific contributions. A second group are those that provide information for the clinician in his evaluation of diagnosis and treatment. A final group are those cases that offer an educational advantage for physicians in training.

If the autopsy is a research type, it should be performed in a detail beyond the so-called classical autopsy technique mastering all applicable aspects of basic science such as biochemistry, microbiology, histochemistry, electron microscopy, to answer pertinent questions regarding disorders that are poorly understood, such as certain genetic diseases, hemorrhagic fever, human homografts, and others.

Obviously the teaching autopsy for the pathologist in training must follow meticulous techniques. He needs to recognize the need for a comprehensive scientific approach to the problem presented and have a full understanding of the modern purposes of a necropsy. If instead they are exposed to repetitious, post-mortem examinations from which they learn little after the first few experiences, they will lose interest as the student already has in many instances. Instead the pathologist in training needs to be challenged with necropsies of unusual importance and this of course must be under the careful guidance, supervision, and review of the experienced pathologist.

Autopsies performed on the unusual case will encourage collaboration between the clinician and the pathologist before the autopsy is performed. It will help to evaluate the clinical data and indicate the category of autopsy procedures to be followed. Such collaboration will make it possible to state whether the patient died of a probable known disease with expected course, whether there were clinical or other aspects requiring an explanation or whether the patient had a baffling and incompletely understood disorder requiring a research effort to obtain the desired complete information.

Apart from research we must not forget that the autopsy does make possible answers to various specific questions and provide simple factual data important for the physician, the family, the statistician and the law. For example, did the patient have peritonitis following an operation? Was a sudden death due to embolism, myocardial infarction or ventricular fibrillation following inhaling of toxic substance or electrocution or drowning? It is recognized that answers to such questions do not constitute science, do not advance conceptual or general knowledge. But they help the overall care of patients.

However, the usefulness of some autopsies is often minimal or nonexistent. The specific answers which an autopsy can provide may often be derived from other sources. Autopsies need not be done merely for the sake of going through certain habitual motions. We all know how the "unfinished" autopsies pile up in the pathologist's office. Some get finished so long after prosecution that no one today cares except the file clerk who can then make an appropriate check mark on a folder or card. These facts expose the popular idea that the more autopsies we do the better off we are, as a pure myth or fetish.

If the autopsy seems to be falling behind in its appeal to physicians or students, it will not meet the competition of other disciplines by standing in the tradition of fifty years ago. This problem was stressed by each participant in the symposium.<sup>1-6</sup>

We cannot give up the autopsy. It is absolutely necessary but it must seek its place among all the various methods of study of the patient, of groups of patients, in teaching or in medical research.

L.H.N.

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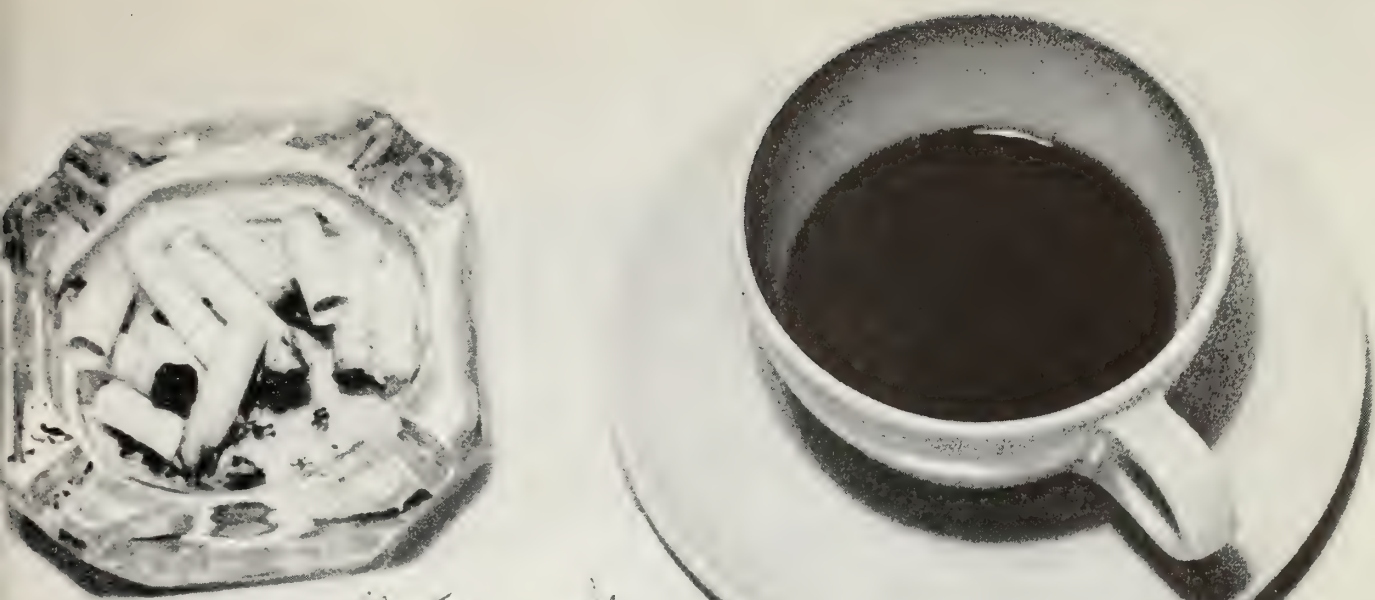
## The Syndrome Of Mesenteric Arterial Insufficiency

The kidneys and the gastrointestinal tract receive together over 50 per cent of the total cardiac output, but they are less vulnerable to short periods of anoxia than the brain or heart. Accordingly they play a major role in supporting levels of arterial pressure whenever factors arise that tend to lower it. Blood diversion from the mesenteric system and the kidneys to the general circulation has long been recognized as a major factor in maintenance of arterial pressure. Accordingly, the more the general circulation is in trouble, the more angiospasm one finds in the mesenteric vascular bed. The sudden factors that tend to reduce blood flow by producing a fall in arterial pressure are hypotension from whatever cause such as hemorrhagic and endotoxic shock, or from acute myocardial infarction and certain cardiac arrhythmias. There also are slowly developing causes for reduction in blood flow such as cardiac failure and mesenteric arterial insufficiency.<sup>1,2</sup>

Up to the present time information on actual blood flow through the mesenteric system has been limited because routine sampling of the portal blood stream has been impossible. We know that the mesenteric circulation is a system rich in anastomatic networks with a low resistance, high flow, and moderate a-v oxygen extraction at rest (4.9 ml oxygen per 100 M.L. blood), these data having been obtained from animal studies.<sup>3</sup>

The clinicians interest in the mesenteric circulation in man derives from two important observations. In one mentioned in the first paragraph, that necrotic changes of the digestive tract have been noted in prolonged serious reductions in blood flow to this area from systemic causes. Marston<sup>4</sup> has analyzed and published information on cases of acute fulminating necrotic bowel lesions, especially in middleaged men and which often follow





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an illness associated with hypotension and vasoconstriction peripherally. The lesions have been given a wide variety of pathological labels such as necrotic jejunitis, acute enterocolitis, pseudomembranous enterocolitis, necrotizing colitis, hemorrhagic duodenitis. They probably result from arteriolar spasm of the bowel wall vessels initiated by any factor producing hypotension. The lethal factor in shock is the occurrence of necrosis of the gastro-intestinal mucosa because of a strangulation of the circulation in this area by excessive and prolonged vasoconstriction.<sup>2</sup>

The second factor that has aroused the clinician's interest in the mesenteric circulation is the finding of a high incidence of atherosclerosis in the vessels serving the bowel. Reiner's<sup>5,6</sup> injection studies of post-mortem specimens have outlined patterns of atherosclerosis that most often involve the celiac, splenic, superior, and inferior mesenteric vessels, as well as narrowing of the sub-branches of these vessels. He found lesions present in 77 percent of his unselected series of autopsies. The incidence of atherosclerosis was as expected higher in diabetes. Furthermore, the occurrence of atherosclerosis in the mesenteric system seemed to be parallel with the severity of arterial disease in the aorta and coronary arteries.

The mesenteric system seemed capable of developing good collateral flow because the obvious degree of atherosclerosis did not necessarily correlate well with the presence of ischemic lesions in the bowel wall. We are well acquainted with this phenomenon in the same lack of correlation occasionally occurring between cerebral and coronary atherosclerosis and the presence of manifest symptoms. It is also established that the symptoms most often due to small bowel ischemia occur when the development of collateral supply is unable to keep pace with progressive narrowing. It is interesting that the stomach is not as vulnerable as is the bowel and infarctions of the stomach are rare in man.<sup>7</sup>

It is not surprising that the pain of mesenteric vascular insufficiency can be confused with symptoms arising from the more common gastric, pancreatic or biliary diseases. The diagnostic difficulty is compounded because of the frequent concurrent but unrelated presence of lesions in these structures in older people. But we must carry with us a high index of suspicion when a patient suffers pain after eating sometimes developing immediately but present at least 30 minutes after eating, the hallmark of the syndrome of mesenteric vascular insufficiency. The pain is generalized or periumbilical although occasionally localized to one of the quadrants of the abdomen. If to the left quadrant, one would suspect insufficiency of the inferior mesen-

teric artery distributed to the left colon.<sup>8</sup> The pain may even radiate to the back and most often is colicky in nature.

The duration of the pain may be from one to several hours, sometimes continuing to the time of the next meal. Motility disturbances varying from distension to nausea, vomiting, diarrhea or constipation, often accompany the period of pain. The only consistent relief is obtained by not eating although reduction in the size of the meal may bring relief early in the course of the disease. Once the food intake is reduced, weight loss sets in and may be pronounced. This is compounded by failure of absorption from the part of the bowel suffering from ischemia. Drugs seem totally valueless.<sup>3</sup>

The course is relentless with increasing pain and eventually acute bowel infarction, usually involving the small bowel, right colon, and a portion of the transverse colon all supplied by the superior mesenteric artery. We get little help from various studies except for an occasional deficiency pattern or abnormal motility pattern. It's clear enough that the diagnosis of mesenteric vascular insufficiency depends upon clinical awareness of the disease and urgent steps to properly perform angiographic studies. This should not be too difficult if the tip of the aortic catheter is close to the orifice of the mesenteric artery so that dye injection may definitely establish the presence or absence of patency. There has also been recently described a radioactive technique for obtaining flow curves utilizing an intravenous injection of a short-range beta emitter and a geiger counter placed in the bowel lumen.<sup>9</sup>

Once infarction has occurred, the mortality is almost 100 percent although a few spectacular successes have resulted from surgical restoration of blood flow combined with resection of the infarcted area.<sup>10,11</sup> Obviously one must try to make the diagnosis in the patients showing the chronic or prodromal symptoms. For in these cases endarterectomy or bypass surgery offers the best chance for long term survival. There is here a real opportunity for early diagnosis because 50 percent of patients with acute bowel infarction secondary to mesenteric thrombosis experience pain weeks to months preceding the acute episode.

We must bear in mind that extensive atherosclerosis may be present without symptoms and we need to have a satisfactory method to establish what is the blood flow and what are the alterations in the mucosal pattern during ischemic stress. Hopefully future work will provide diagnostic techniques that have the usefulness of the electrocardiogram in the diagnosis of abnormalities of blood flow in the mesenteric system.

L.H.N.

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## Ethical Problems In Human Experimentation: 1. In Relation To Law

The ethical problems of human experimentation was admirably discussed last spring at Harvard by the distinguished jurist, Paul A. Freund, Carl W. Loeb, University Professor at the Harvard Law School and President of the American Academy of Arts and Sciences. He points out that the law of medical experimentation has not crystalized into firm neat rules and therefore the law cannot be expected to yield precise answers to the ethical problems of medical experimentation. He believes there will have to be a closer interchange between medicine and law so that each discipline will have to clarify the issues in the light of its own experiences and its own ways of thinking. In any such dialogue it becomes necessary for the physician to understand certain characteristics of the legal process and the legal mind, and it will be necessary for the legal profession to understand the doctors problems in his search for the best ways of curing his patient and his aim to advance knowledge so that other patients and future generations will benefit from his present experience.

Professor Freund points out certain of the several characteristics of the legal process and the legal mind. First of all the law is conservative. Justice Holmes long ago pointed this out that continuity

with the past is not a duty it is a necessity. This is why the law is addicted to principle and adheres to it for it constantly fears a bad precedent. The law takes refuge in general rules as metaphysics resorts to absolutes.

Not only is the law conservative, but it is deeply protective of human integrity and human life. An offensive touching or invasion of the body if not consented to is a trespass against the person, a battery that can be redressed in an action for damages. If a human life is taken deliberately it is no mitigation of the crime to claim that the victim was by worldly standards someone of little merit or someone having little time to live. In short, the governing standard is not the merit or need or value of the victim but equality of worth as a human being. In short the governing principle is that man shall not play "God" with human life. Even the saving of lives will not justify the taking of a life except in self defense or in defense of a third person.

Besides being conservative and sensitively protective of human life the law Professor Freund points out, is also dialectical in method. The adversary system that is at the heart of our law assigns roles to the advocates, to the judge, and it would disrupt the system if anyone attempted to play a role other than his own. For example, if the advocates attempted to take the place of the judge and himself be judicial, the system would break down. Thus we come to recognize that each advocate owes perfect loyalty to his client within of course the proprieties of honor and of the system.

This dialectical aspect of the law has led not only to the conservation of the law but to its being both creative and responsive to the needs of society. Just as the law has raised up a right of privacy which is a creative innovating doctrine, so it may come to recognize a right of experimentation as human beings. For social interests and expectations such as need for obtaining cures for such human scourges as cancer and heart disease, are certainly justified and can eventually be reflected in a law that would allow certain types of human experimentation to the end of protection of present and future human life. For both the interest of society and a religious or semi-religious view of the dignity of human life lead to a concern to serve humanity.

The law has indeed yielded in its absolutes where some worthy risk has pressed for acceptance. Professor Freund points out that we can calculate pretty well the risk of mortality for 1,000 autos on the road or 1,000 drivers under age 20 and yet we permit the autos and young drivers on the highway. We take the risk. We can calculate the loss of life in any large scale job of highway construction or tunneling or the building of skyscrapers and yet we



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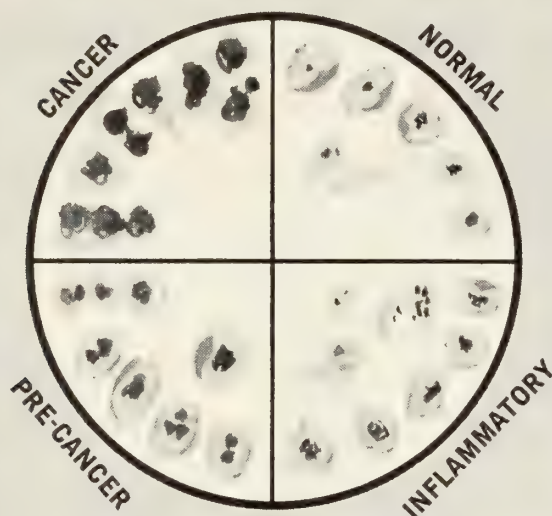
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The crux of the matter is to find the inner checks or other safeguards that will mitigate and justify the risk be it in industry or be it in medicine. The law on the whole subject of experiment will be worked out in close reliance on the moral sensibilities of the community. As far as medical experimentation is concerned the medical profession will have to take the public into its confidence and to educate the public, rather than risk the shock and explosion of pent up revulsion such as occurred when the public discovered that patients were being inoculated with cancer cells even though it was a harmless and benign procedure.

Professor Freund thinks the primary step is to recognize that different moral problems and moral dilemmas do exist in which help and guidance must be sought from many sources especially the medical profession. He points out however that there are times when even moral practices break down as for example the Nazi experience in which well human beings were maimed or killed by "high standing" physicians whose hideous pathological attitude justified their crimes by quoting the welfare of the species as over-riding that of the simple man. However they chose for their involuntary victims well persons that they considered belonging to an "inferior race."

In ethics and biology we may learn from pathological specimens. In the end we may have to accept the fact that some limits do exist in the search for knowledge. And we must rely on the wisdom and age old tradition of the medical profession in its dialogue with the legal profession to set rules and boundaries in human experimentation.

L.H.N.

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## The Forgotten Sick Man— The Alcoholic

Elsewhere in this issue (see page 119) Dr. Terhune points out that the alcoholic suffering like other addicts from a malignant disease does not willingly give up the drug and that when all other procedures fail, the Connecticut Legislature has provided a wise and humane measure to enable families to place such patients under enforced medical treatment for long enough to get results.

This subject is obviously of such importance that it gave rise to a three-day national conference in June, sponsored by the Boston University Law-Medicine Institute to examine the legal issues in alcoholism and alcohol usage. Present were leaders of the judiciary, the law schools, the medical profession, the forensic sciences, law enforcement and correction, as well as representatives of alcohol treatment programs. This conference is excellently reported by N. L. Chayet.<sup>1</sup> He summarizes the important themes considered at the Conference. One was a discussion of when the law should exercise its coercive power to institutionalize the alcoholic patient against his will.

This theme was very well analyzed by Professor William J. Curran in a paper entitled *Civil Commitment of Alcoholics*. His legal survey pointed to the lack of uniformity throughout the United States on the legal basis of commitment. Apparently the definition of the committable patient varies significantly from state to state. In most states the alcoholic to be committed must have "lost his self-control." However, there appears no uniformity in the qualities that are listed along with self-control. In some it is "addiction" to alcohol for a specific period usually one year. Then there may be inability to handle one's property, or danger to the community, danger to one's self, and a certain number of arrests for drunkenness. In California the law incorporates practically all of these elements; In Minnesota the sole criterion for commitment is "inability to manage one's affairs."

Professor Curran believes that involuntary commitment is over-used for too wide a class of alcoholics. Sweeping alcoholism into these institutions "creates an illusion of coping with a great public health menace." Accordingly one of the conference recommendations was "That the machinery of civil commitment be brought to bear only when an individual constitutes a danger to the public at large."

A question was raised at the conference as to whether all persons committed to institutions through regular channels actually belong in mental institutions. There was quoted evidence that as many as a third of all admissions to mental hospitals are for alcoholism (31.4 percent in Maryland during 1964). A question was raised as to whether the physician who is asked to certify an alcoholic patient for the purpose of involuntary commitment has any alternative to such action or is he forced by a rigid statutory scheme to take such action because there is no provision for alternative methods of handling the problem.

Judge W. H. Burnett of Denver described the successes of a method of handling drunken offenders in the Denver Court. The method "seeks to

balance threats and penalties with a helping hand." The program employs the unique policy of releasing a defendant before his court appearance whenever possible and makes provision for a voluntary court honor class which is a blend of discussion and lecture series for the offender designed at motivating him to cease his drinking pattern through use of tactics similar to those employed by Alcoholics Anonymous.

A good deal of discussion and interest focused on the cases presently in which attempts to examine whether the victim has committed a crime or suffers from a disease. Arguments were presented that such a person should not be found guilty of drunkenness because he is not responsible owing to his illness and that he cannot form a "guilty mind" required for a crime. On the other hand Dr. Nils Christie of Norway thinks their method of many fines for drunken driving has generated a respect for drinking driving legislation which apparently is nonexistent in this country.

Perhaps the most important recommendations emanating from the conference were those aimed at awaking the professions of law and medicine to the problem of alcoholism and alcohol usage and to take active steps to do something about this problem. We need to have more knowledge on alcoholism and alcohol usage, the relation of drinking and driving, family break-up and similar areas of widespread legal and social significance. Accordingly, the conference recommended that the American Bar Association and the American Medical Association establish a joint committee to study these problems and that such committees include representatives of all groups in medicine and law that have an interest in this area.

One thing did become clear at the conference: the fact that doctors and lawyers alike need to know more about alcoholism as a disease and about how to deal with those who are its victims. There is need for speedy action and intensive research. Dr. Terhune's article in this issue opens the door.

L.H.N.

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## Phenylalanine And Chloramphenicol

Chloramphenicol is an excellent antibiotic especially in hemophilus influenza, salmonella and E. coli infections. At the same time it has been used

with caution and trepidation because of its well known effects upon the hematopoietic system leading to aplastic anemia in some patients. How to be able to use it and at the same time avoid its complications has been the big problem in therapeutics.

Our present practice when administering chloramphenicol is to take frequent blood counts and on the first appearance of anemia to discontinue the drug. This practice is clearly unsatisfactory, but is the only one generally available to use. It is unsatisfactory just because what is happening in the bone marrow precedes by days the evidence of damage in the peripheral blood. In fact, Ingall, et al.<sup>1</sup> describe a case in which the first sign in the peripheral blood was a hemoclastic crisis requiring immediate transfusion with packed red cells. Thus only following the picture in peripheral blood can lead to disastrous consequences. It is also unsatisfactory because once evidence of damage to the erythroid elements appears, the antibiotic must perforce be discontinued even though its therapeutic benefits may not have been achieved. Clearly we need to know more about the way in which chloramphenicol causes damage to the erythroid elements and how to prevent them.

Ingall, et al. studied the bone marrow of 8 infants and children who were receiving chloramphenicol for E. coli, Salmonella and hemophilus influenza infections. They noted as did others before them,<sup>2</sup> that early in the development of chloramphenicol toxicity vacuoles appear in the erythroid and myeloid precursors in the bone marrow. Similar cytoplasmic vacuoles in the erythrocytes have been reported in other conditions such as erythremic myelosis, acute alcoholism and especially in infants suffering from phenylketonuria receiving a phenylalanine deficient diet. It is relevant to this discussion that the vacuolization of the erythroid elements in such infants disappeared when phenylalanine was added to these infant's diet.

Back in 1950 Woolley<sup>3</sup> had noted that, in-vitro, phenylalanine inhibited the antibacterial effect of chloramphenicol upon E. coli. Could phenylalanine also inhibit the toxic effects of chloramphenicol upon the bone marrow in-vivo without affecting its antibacterial activity? This thought together with the observation that phenylalanine prevents vacuolization of the erythroid elements in phenylketonuria, led Ingall, et al.<sup>1</sup> to study the bone marrow of 8 infants who were treated with chloramphenicol for serious infection. The most striking findings were the presence of vacuolization in the erythroid elements in three of the patients. They were most numerous in the erythrocytes and A normoblasts. The vacuoles were cytoplasmic, round and of variable size. In these three, who were



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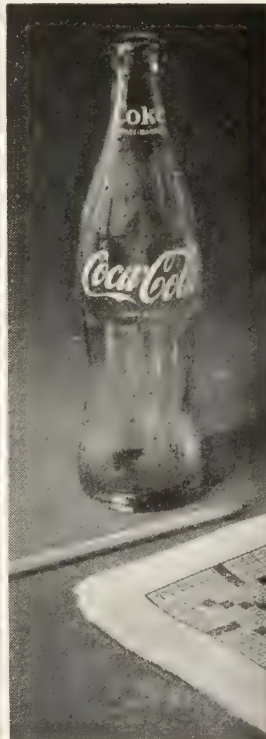
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also the sickest, the chloramphenicol was continued, but with the administration of phenylalanine for 2-4 days the bone marrow returned to normal.

There was no correlation between the average or individual concentrations of chloramphenicol and the morphologic appearance of the bone marrow. The doses of phenylalanine administered were small and the duration of administration short. Nonetheless the effects were dramatic in the three patients treated with phenylalanine and they recovered from the infection as well as the vacuolization of the erythroid elements in the bone marrow.

Further study is needed to determine the efficacy in patients with more advanced bone marrow disturbances produced by chloramphenicol. In the meanwhile it seems reasonable that a trial of phenylalanine administration should be attempted in patients at various stages in the development of bone marrow hypoplasia from chloramphenicol and even after hypoplasia has been fully established, since it is clear from Ingall, et al. studies the phenylalanine can reverse the toxic effect of chloramphenicol upon the erythroid elements.

There is one point that needs further clarification. That is whether the antagonism of phenylalanine to the toxic effects of chloramphenicol on the bone marrow is not accompanied by an equal antagonistic effect to the antibacterial activity of chloramphenicol. In Ingall's study the three patients with bone marrow changes did recover from the infection even though phenylalanine was administered. However the amino acid was given only after the sixth day of chloramphenicol administration and the infection may already have been conquered even though the bone marrow showed toxic effects. What would happen to the infection if phenylalanine were to be used from the start of chloramphenicol administration is of course unknown and requires urgent clarification.

What we do know is that if evidence of bone marrow toxicity appears in the course of chloramphenicol therapy, it can be controlled and toxic effects reversed by the use of phenylalanine.

L.H.N.

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## An Up To Date View Of Thrombo-Embolism

Autopsy studies at the Peter Bent Brigham Hospital in Boston revealed pulmonary embolism to be the most single common cause of death.<sup>1</sup> It is not surprising therefore that in the last 5 years, the field of venous thrombo-embolism has seen more progress than at any time since the introduction of anticoagulants 20 years before. Much of this has come from useful diagnostic procedures introduced, such as measurements of enzymes of the blood, pulmonary angiography, pulmonary scanning after injection of radioactive albumin and clot detection after tagging with radioactive fibrin or plasminogen.

New treatments have appeared in the form of thrombolytic agents to dissolve clots and surgical operations for their removal from the leg veins (thrombectomy). There have been new understandings in terms of anticoagulation dosage, vena cava ligation or plication, and more recently with the development of open heart surgery attempts at pulmonary embolectomy. Although significant advances have been made in the areas of pathogenesis and diagnosis, the treatments offered for thrombo-embolic disease remains controversial. Therapeutic evidence has been offered, as Thomas<sup>2</sup> points out. Some of it has been with an experimental basis. Some has been lacking in clinical sense and the bulk has been woefully deficient in both.

In venous thrombosis, the thrombus is more akin to a blood clot and is red, while in arterial thrombosis, the fundamental event appears to be an initiating platelet nidus. To avoid the red thrombus, therapeutic attempts revolve first around reducing venous stasis in the legs. Second is the need to counter an assumed systemic hypercoagulability. It is now known from experimental observations on animals that venous thrombi neither form nor propagate if the animals are given sufficient intravenous heparin to prolong the glass clotting time to greater than twice normal. In addition heparin may also have an important function in the treatment of pulmonary emboli by preventing the airway constriction which in the absence of heparin, occurs because of release of serotonin locally. Thomas<sup>2</sup> in his excellent review of this subject points out from clinical reports that fatal pulmonary embolism is very uncommon once a large dose of heparin (40,000 units per day) has been administered intravenously.

Certain patients are notoriously liable to have pulmonary emboli, the so-called high risk group, such as elderly patients with fractures at the neck of the femur, those forced to be in casts for over three days or those with congestive heart failure. Pru-

dence would demand that such patients should be treated prophylactically, although there is always the need to strike a balance between indiscriminate administration of anticoagulants to every patient admitted to a hospital and its too narrow restriction. Much information has accumulated that anticoagulant therapy in such high risk cases greatly reduces the incidence of pulmonary embolism. At the same time one must bear in mind that the hemorrhagic complications of anticoagulation treatment are real and many endanger life owing to difficulty in supervising variations in patients sensitivity, mistaken dosage, and laboratory errors. This is more true for ambulatory patients than those in a hospital.

When it comes to treatment of overt pulmonary embolism, Thomas points out that by using intravenous heparin, the mortality rate can be greatly reduced quoting Barrett and Jordan who reported an important reduction in death from pulmonary embolism from 26 to 2.2 percent by using intravenous heparin. One point not settled is whether subcutaneous or intramuscular heparin can be as effective as the intravenous route. One thing however is certain, that prompt treatment can prevent the recurrent showers of small emboli found especially in post-partum women, which can lead to pulmonary hypertension and right heart failure if anticoagulation therapy is not given promptly.

Over the years the development of surgery for thrombo-embolic disease has ranged from superficial femoral ligation to common femoral ligation, to vena cava ligation or plication and finally to pulmonary embolectomy. Thomas clearly points out the advantage of vena cava ligation as opposed to more distal venous ligation and the small advantage if any of vena cava plication over ligation. There is also a widening recognition of occasional later embolism via the huge collaterals that occur after inferior vena cava ligation. A study of the pathophysiology of pulmonary embolic disease forces upon us the question as to the long term effectiveness of venous ligation which may prevent massive emboli but not multiple small emboli nor diffuse microemboli which gradually occlude the pulmonary vascular bed. Obviously to prevent these complications patients will have to remain on chronic anticoagulation for prolonged periods even after surgery.

Open heart surgery has made possible pulmonary embolectomy. Numerous case reports of successful embolectomies have appeared in recent literature. Thomas intimates that even in massive emboli, immediate heparin therapy may be life-saving. His argument is that although some patients may be saved by embolectomy since one-fifth of such

patients live long enough to permit the operation, the crux of the issue is however the decision when to operate. If the patient fails to respond to conservative measures such as oxygen, morphine, heparin, within minutes then recovery is unlikely. The great challenge is the decision to proceed with operative intervention in critically ill patients some of whom will recover spontaneously. This challenge is especially great, since there is evidence that intravenous heparin represents a highly effective mode of treatment in the patients who do not die immediately from massive pulmonary embolism. This view is not specifically documented and of course is not widely accepted by the cardiac surgeons who believe there are some patients in whom pulmonary embolectomy is the only life saving measure available. The trick of course is to decide which are these cases. At this stage in our knowledge Thomas's word of caution about the dangers of the indiscriminate application of pulmonary embolectomy is indeed needed.

The major hazard to patients with peripheral venous thrombosis is of course pulmonary embolism. A patient with overt thrombophlebitis is clearly in a high risk category in relation to the possibility of embolism. Any overt evidence of thrombosis means the patient may be in a thrombotic state with a propensity of forming thrombi at other sites. In fact such a patient may also have a concomitant silent deep venous thrombosis. It would seem therefore logical to regard the presence of thrombosis in an acute form at any site as an indication of the existence of a thrombotic state which should ipso facto be treated with prophylactic anticoagulant therapy. Such treatment will prevent propagation of a thrombus, but more important is the fact that it is also prophylactic treatment for pulmonary embolism. Thomas does not consider the important therapy (thrombectomy) of venous thrombosis in the leg that concerns the prevention of post-phlebitic leg edema. Nor does he consider thrombosis in a varicose vein among the 20 percent of cases of superficial phlebitis in which there is a concurrent concomitant deep phlebitis. Shall these be excised or treated by anticoagulant therapy?

L.H.N.

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In clinical trials, Eutron produced normotension or a significant reduction in blood pressure in eight out of 10 patients studied. The rationale for the product is this: Eutonyl used alone is a potent antihypertensive. Its antihypertensive action is markedly enhanced by Enduron, a potassium-sparing thiazide.<sup>1,2,3</sup> The combination (Eutron) thus produces greater antihypertensive effect with lower dosages of the Eutonyl component, and milder side effects may be seen.

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BP reductions in the recumbent and sitting positions often are nearly as great as in the standing. In clinical trials, the average *recumbent* BP reduction was 36/18 mm. Hg.



The average *standing* reduction in clinical trials was 45/22 mm. Hg. Thus the difference between the standing and recumbent readings was only 9/4 mm. Hg.



## Significantly lowers blood pressure in all body positions; less likelihood of orthostatic hypotension

In clinical trials, the average reduction in standing blood pressure was 45/22 mm. Hg.; in the sitting position it was 48/20 mm. Hg.; and in the recumbent position, 36/18 mm. Hg.

Because Eutron effectively reduces blood pressure in all body positions, there is reduced likelihood of orthostatic symptoms or hypotension.

This was reflected in the relatively mild character of side effects seen in clinical trials (see below).

### Smooth and gradual onset

Onset of antihypertensive action is usually quite smooth. Initial reduction of systolic and diastolic readings is usually seen within a week — maximum reduction in seven to ten days.

## Less troublesome side effects may be seen; frequent improvement in “sense of well-being”

Fewer than 1% of patients studied discontinued Eutron therapy because of side effects. This is due in part to the relatively low dosage needed with the combination. Usual recommended dose is one tablet daily—that is, 25 mg. Eutonyl with 5 mg. Enduron. *This is about half the usual therapeutic dose of Eutonyl given alone.* As a consequence side effects may be milder. And, as with Eutonyl given alone, the patient may well note an increased sense of well being. This is in distinct contrast to most other antihypertensive therapy.



# Prescribing information for **EUTRON**

**INDICATIONS:** Eutron (pargyline hydrochloride and methyclothiazide) is indicated in the treatment of patients with moderate to severe hypertension, especially those with severe diastolic hypertension. It is not recommended for use in patients with mild or labile hypertension amenable to therapy with sedatives and/or thiazide diuretics alone.

**CONTRAINDICATIONS:** Eutron is contraindicated in patients with pheochromocytoma, advanced renal disease, paranoid schizophrenia and hyperthyroidism. Until further experience is gained it cannot be recommended for use in patients with malignant hypertension, children (under 12 years of age), or pregnant patients.

The concomitant use of the following is contraindicated: other monoamine oxidase inhibitors; parenteral forms of reserpine or guanethidine; sympathomimetic drugs; foods high in tyramine such as cheese; imipramine and amitriptyline, or similar antidepressants; methyldopa. A drug-free interval of two weeks should separate therapy and use of these agents.

**WARNINGS:** Pargyline hydrochloride is a monoamine oxidase inhibitor. Patients should be warned against eating cheese, and using alcohol, proprietary drugs or other medication without the knowledge of the physician. When it is necessary to administer alcohol, narcotics (notably meperidine), antihistamines, anesthetics, barbiturates and other hypnotics, sedatives, tranquilizers, or caffeine, these agents can be used cautiously at a dosage of  $\frac{1}{4}$  to  $\frac{1}{2}$  the usual amount. Avoid parenteral administration where possible. Withdraw pargyline two weeks before elective surgery.

Patients should be warned about the possibility of postural orthostatic hypotension. Those with angina or other evidence of coronary disease should not increase physical activity. Pargyline may lower blood sugar. Potassium depletion is unlikely at the recommended dosage, but if it occurs, adjust dosage or withdraw or provide added natural food sources of potassium; potassium tablets should be avoided wherever possible, as bleeding or obstructive ulceration of the small bowel has

been associated with their use; potassium levels should be especially watched if the patient is on digitalis or steroids, or if hepatic coma is impending.

**PRECAUTIONS:** When determining the anti-hypertensive effect of Eutron, blood pressure should be measured while the patient is *standing*. Use with caution in hyperactive or hyperexcitable persons. Such persons may show increased restlessness and agitation. Withdraw drug during acute febrile illness. Watch patients with impaired renal function for increasing drug effects or elevation of BUN and other evidence of progressive renal failure; withdraw drug if such alterations persist and progress. Pargyline has not been shown to cause damage to body organs or systems. As with all new drugs, complete blood counts, urinalyses, and liver function tests should be performed periodically. The drug should be used with caution in patients with liver dysfunction. With prolonged therapy, examine patients for change in color perception, visual fields, and fundi.

Elevated blood urea nitrogen, serum uric acid or blood sugar are possibilities attributable to the methyclothiazide in Eutron. Methyclothiazide may also reduce arterial response to pressor amines. Blood dyscrasias, including thrombocytopenia with purpura, agranulocytosis and aplastic anemia, have been seen with thiazide drugs.

**SIDE EFFECTS:** The use of pargyline may be associated with orthostatic hypotension. Mild constipation, slight edema, dry mouth, sweating, increased appetite, arthralgia, nausea and vomiting, headache, insomnia, difficulty in micturition, nightmares, impotence, delayed ejaculation, rash, and purpura have been encountered with pargyline. Hyperexcitability, increased neuromuscular activity (muscle twitching) and other extra-pyramidal symptoms have been reported. Drug fever is extremely rare. Congestive heart failure has been reported in a few patients with reduced cardiac reserve. Nocturia has been observed with the combination. If side effects persist, despite symptomatic therapy or reduction of the dose, discontinue the drug.



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## Mutual Medical-Dental Problems: The Prevention Of Dental Disease By Diet

Two disease lead to wholesale loss of teeth, dental caries and periodontal disease. The former is widespread in this country and in Britain.<sup>1</sup> The latter is extensive in many underdeveloped countries and also in this country.<sup>2</sup>

The development of sound caries resistant teeth is dependent upon an adequate diet during fetal and early life. Because our diets are generally plentiful and nutritious, malnutrition is uncommon as are mineral and vitamin deficiencies. Fluorides do prevent much of dental caries and any deficiency of fluoride intake can be and is being corrected in many parts of this country by fluoridation of water supply. But even with fluoridation there will remain a goodly number of children who will develop caries. It is therefore important to consider other causes of caries besides mineral deficiency.

There is growing evidence which implicates production of acid in the mouth as a major factor.<sup>3</sup> There is also strong evidence that carbohydrate provides the substrate from which the acid is produced by oral microorganisms. For caries to develop as a result of acid in the mouth two things are necessary—acid in adequate concentration, and time for the acid to act on the tooth enamel. Only disaccharides and monosaccharides are broken down rapidly enough in the mouth to cause damage. The polysaccharides are swallowed before they are degraded, but the simpler sugars usually consumed in the form of cakes or confectionaries which stick around and between the teeth for up to an hour are broken down to acid within a minute or two. This acid tends to be buffered by the saliva and would not harm the teeth were it not for dental plaque. Plaque forms like a scum on the surfaces of teeth, especially in areas such as the fissures and between the teeth where cleaning and friction of mastication have little effect.

Studies with microelectrodes<sup>3</sup> have shown that after consumption of a fermentable carbohydrate a pH gradient develops in the plaque. The outer layers are affected by the saliva and remain at or about pH7. In the "inner layers" however where the plaque is against the enamel, the pH falls to 5 or below and remains so for half an hour. At these low pH levels, enamel is attacked and caries develop even though the plaque may contain fluoride.

The practical implications of these basic studies were investigated in the now classical Viperholm Study in Sweden. One group of subjects were given a nutritionally adequate diet low in sugar while

other groups were given the same diet with various supplements of carbohydrate and sugar. They found that the total quantity of sugar consumed seemed not to have a great effect on the incidence of dental caries. What was important was the frequency of consumption.

Subjects who consumed sugar between meals especially in the form of sticky toffies had vastly more caries than did those who consumed an equivalent amount of sugar at meal time. Further work has shown that children who are not given snacks between meals have far less caries than similar children who eat between meals. Snacks are usually of carbohydrate with low nutritional value and tend to spoil the appetite for the more nutritious foods consumed at meal time. Thus from every point of view eating between meals is certainly to be condemned.

Periodontal disease which is so widespread in many underdeveloped countries develops in part because the plaque which tends to form on teeth is not removed frequently enough. There develops toxins from the bacteria in the plaque which seep down into the crevices between the gum and the tooth and thence through the epithelium to the underlying connective tissue. It seems not feasible to remove the plaque often enough to prevent the toxins from forming. Though of low grade these bacterial products lead to the progressive destruction of the collagen fibers and alveolar bone supporting the teeth. The crevice between the gum and tooth becomes deepened to form a pocket in which more bacteria can proliferate to accelerate the process.

The British Medical Journal editorial points out that periodontal disease is closely related to diet and its refinement even if it is not due to acid formation. However the consistency of the diet, its tendency to stick around the teeth is important. Our modern diet tends to be overcooked, soft, sticky and designed as a cynic has said for "a nation with ill fitting dentures." To prevent that aspect of periodontal disease caused by diet, it will be necessary to prevail upon our patients to eat foods which need chewing. These of course are largely fresh fruits, vegetables and certain protein foods.

It is clear that a part of dental caries and periodontal disease is caused by the wrong diets. This part can be prevented by a diet which needs chewing and is eaten only at meal times, eschewing sticky sweets taken also in between meals.

L.H.N.

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## Medical Complications Following Cardiac Operations

There has been a steadily increasing number of patients undergoing corrective cardiac operations. This is due to great improvements in the techniques employed by the cardiac surgeon. The dramatic improvements publicized in the lay press in some patients who have successfully emerged from the cardiac operation has produced a sympathetic public. The physician who refers a cardiac patient for surgical evaluation of the possible benefits and hazards of a cardiac operation however bears some responsibility, however slight, for the outcome if an operation is performed and he should become aware of the incidence of operative and post-operative complications that may be expected. In practice it turns out that there are numerous complications of a medical nature following operations on the heart and great vessels, but because they are managed by the expert team of cardiac surgeon and medical associates, the referral physician remains somewhat uninformed about the incidence and management of "medical" complications his patient may have undergone following a heart operation.

Williams, Morrow and Braunwald<sup>1</sup> have just published an informative paper on an analysis of the incidence and management of "medical" complications following cardiac operation. It turns out that although there have been improvement in direct mortality associated with operations on the heart and great vessels, that complications secondary to the operation usually occurring in the early post-operative period may still represent serious threats to the patient's survival. These complications involve disturbances in cardiac rhythm and contractile state, electrolyte balance as well as in the function of renal, gastro-intestinal, pulmonary, hepatic, hematopoietic and the central nervous system.

Because of the nature of these complications, they are managed most effectively by the combined efforts of internist, cardiologist, and surgeon and are termed "medical complications" of cardiac operations. Some are seen only in the immediate post-operative period and the manifestations and management may be quite different than when they are found in patients not yet operated upon. Williams' paper presents the analysis of 150 adults who were operated upon for a variety of lesions at the National Heart Institute, survived the opera-

tion and returned to the intensive care unit. The complications that occurred before the patient's discharge from the hospital were analyzed.

A total of 187 complications occurred in 107 patients and were directly responsible for the death of 15. No such complications occurred in 43 others. Serious arrhythmias are a frequent occurrence after cardiac operations. Ventricular extra-systoles were so common in the early post-operative period especially following valve replacement that they were not even included in this complication. But as we all know, they can be the harbinger of ventricular tachycardia or ventricular fibrillation. The causes generally were digitalis toxicity, electrolyte disturbances, hypoxia, acidosis, all of which can generally be corrected with appropriate drug therapy and removal of the exciting cause.

The detection and correction of such arrhythmias was essential since some patients are vulnerable to them. Some patients were found quite vulnerable to the development of severe and possibly irreversible hypotension, and even ventricular fibrillation requiring immediate external electrical counter-shock. It appears also that increased sensitivity to digitalis after operation contributed to serious arrhythmias in some patients.

Five patients developed congestive heart failure or it got worse in those who suffered from this state before operation. They developed hypotension, with cyanosis, progressive metabolic acidosis and four of these patients died. The experienced cardiologist of course seeks some explanation, in cardiac tamponade, hypovolemia, metabolic acidosis and inadequate surgical correction, since these complications must always be kept in mind.

They found many patients with electrolyte disturbances such as hypo- and hyperkalemia and hyponatremia that needed correction. Interestingly enough the authors found the electrocardiogram of limited value in the diagnosis of altered electrolyte states. They found that findings suggestive of electrolyte abnormalities frequently occur after cardiac operations in patients with normal serum potassium levels. Obviously serum determination of electrolytes alone cannot be relied upon to detect abnormalities requiring correction.

Renal complications occurred in seven patients preceded by hypotension in three. The management was to support the blood pressure, appropriate fluid intake and restricting of drugs that the kidney must excrete such as digoxin and streptomycin.

There were five patients with cerebral emboli, a complication that generally followed valve replacement. Three of the patients developed the "madness"<sup>2</sup> syndrome between the fourth and sixth day but recovered.



The most serious complication, more so than shock, was acquired infection. This occurred in four patients and all died.

There were less serious complications such as pulmonary complications requiring tacheostomy. Sixteen patients developed the post-pericardiotomy syndrome, 3 hemolysis, some hemolytic diathesis, 3 gastro-intestinal bleeding and 3 temporary hypertension.

From Williams' analysis of 150 patients undergoing cardiac operations it is clear that medical complications constitute an important, if not the most important, cause of death in patients undergoing heart surgery. Even when non-fatal, these complications add to morbidity and to the length of stay in the hospital. They may result in long-term damage to the organ system involved. The "medical" complications occur more frequently and are more hazardous in the patients who have had a valve replacement since of the 59 patients in whom a prosthetic valve was inserted, 70 per cent of the complications occurred and 73 per cent of the deaths. It is clear that an awareness of the hazards and clinical manifestations of the complications and close cooperation between surgeon, internist, and cardiologist are mandatory if these

patients are to enjoy the ultimate benefits of corrective operative procedures.

The immediate post-operative "medical" complications are important for the referring physician to understand when he refers a cardiac patient to a cardiac surgical team, but he knows this is not the whole story. He knows complications are by no means limited to this period. Indeed, most of the difficulties experienced by these patients following their discharge from the hospital are more of a "medical" than surgical nature. There are the embolizations, hemolytic anemia and hemorrhage resulting from anticoagulants used in patients with prosthetic valves, the development of serum hepatitis, the persistence of myocardial failure, pulmonary hypertension and tricuspid regurgitation. All these are problems that are most frequently encountered and dealt with in the late post-operative period.

L.H.N.

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# The Brain-Damaged Child: A Misconception?

Paul N. Graffagnino, M.D.

■ Many children present a syndrome that falls somewhere in the gray area on the diagnostic spectrum between gross neuromotor disorder and psychiatric disorder. The manifestations of this syndrome may appear on neurologic examination, and in developmental histories, electroencephalographic studies, psychological tests or psychiatric interviews. The child who presents this syndrome is often labelled a "brain-damaged" or "brain-injured" child.

The purpose of this paper is to define and describe this clinical entity, discuss its etiology, outline diagnostic procedure, suggest a program for treatment of the syndrome, and finally to discuss some of the misconceptions that interfere with successful management.

The brain-damaged child is usually defined as a child who presents certain emotional, behavioral or perceptual disturbances with or without positive findings on the neurological examination. It is assumed that the symptoms result primarily from congenital, traumatic or infectious damage to the brain and secondarily, from the interaction of the organically-induced dysfunctions and the environment during the child's psychological development subsequent to the injury.

The term "brain-damaged child" applies to a behavioral pattern rather than to an etiologic or microscopic-pathologic pattern. Among others, Birch<sup>1</sup> believes that "brain-damage" is an "unfortunate diagnostic label" both because it implies a verified etiology where none exists and also because it leads to an overly rigid stereotype of the symptomatic results of cerebral injury. However, since it is clear that many children fall into this clinical and behavioral grouping, "the baby," Birch cautions, "should not be thrown out with the bath water" on the basis of semantic difficulties. Admittedly the term lacks diagnostic clarity, but other labels—the "Strauss syndrome," emotional and psychomotor disinhibition, hyperkinesis, perceptual handicap—have also failed to describe the condition adequately.

The problem of the so-called brain-damaged child has been of interest to educators, school psychologists, clinical psychologists, psychiatrists, pedi-

atricians and neurologists for many years, especially following the early work of Strauss and Lehtinen.<sup>2</sup>

## Clinical Features

Most workers in this field agree that at least three cardinal symptoms appear in the brain-damaged child: impulsiveness, distractibility and restlessness. To these, Laufer and Denhoff<sup>3</sup> add irritability, inability to delay gratification, and other symptoms that interfere with school work. According to Birch,<sup>4</sup> a child of school age diagnosed as having brain-damage syndrome may have been referred for several reasons:

1. Overactive and hyperkinetic behavior that is unpredictable.
2. A short attention span and shifts in the child's ability to perceive the external environment.
3. Extreme emotional lability.
4. Social incompetence revealed in function below the level appropriate for the child's age.
5. Vacillating work habits in school.
6. Impulsiveness and meddlesomeness.
7. Specific learning defects.

The "brain-damaged child" can be a happy, friendly, out-going and smiling child who has winning ways much of the time; yet because of his symptoms, he is viewed as strange and "different" by his peers, his teachers and his family. The addition of this likeableness to the child's variability, unpredictability and impulsiveness seems to increase the frustration of those who participate in his development and education.

## Etiology

It is postulated that the brain-damaged child's characteristic distractibility has its source in his distorted perception of the world. Some authors feel this distractibility has two aspects: the child is inordinately attracted toward irrelevant details so that he loses sight of the whole environment; secondly, he experiences what has been described as a fluctuation in his figure-ground perception. The child's ability to discriminate between an object in the foreground and an object in the background is affected because his perception is poor and shifting. It is assumed that the child's perceptual problems

*Presented at the 182nd semi-annual meeting of the Tolland County (Conn.) Medical Association, October 20, 1964.*

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are the consequence of some structural or neurophysiological defect in the brain. Strauss and Lehtinen<sup>2</sup> believe that the altered physiology of the brain is basically a "disinhibition" of the lower brain centers and that injury to new brain regions releases the more primitive functions of the old brain, particularly in the hypothalamic and limbic regions. The damage to the brain may have been incurred as a result of prenatal, natal or postnatal injury, infection or inflammation; or the malfunction may have been inherited. So far it has not been possible to correlate the clinical symptomatology and the structural damage to the brain in a scientifically valid way.

### Diagnosis

The diagnosis of brain-damage syndrome requires complete study of the child by a team of experts representing several disciplines. This team should include a pediatrician, neurologist, child psychiatrist, psychologist, teacher, and other specialists as indicated. The psychiatrist plays an important role on the diagnostic team. He can create awareness of the need to view brain damage as only a single factor that has to be taken into consideration along with the emotional, developmental, social, biological, environmental and endocrinological factors of the child's life.

It should be emphasized that no one physician or other specialist is qualified to make a diagnosis of brain damage, because no one expert is competent to examine all aspects of the picture without the help of other experts.

Diagnostic procedure should include:

1. A thorough medical history and a review of old records. These may indicate whether an insult to the brain occurred in early life. When such insult occurred prior to the fourth or fifth year of life, the patient presents the picture considered typical of the brain-damaged child. When the injury occurred in later life, he presents a picture that more nearly resembles the description of brain injured soldiers studied after World War I by Goldstein.<sup>5</sup>

2. A careful neurological examination. Minor signs may point to some neurological deviation that might not be evident on routine examination. Findings, for instance, may reveal poor muscle tone, poor coordination of large and small muscles, slight deformation of the hard palate, strabismus, hearing defects, speech defects, increased dependent reflexes, agnosia, alexia or apraxia. Electroencephalographic studies frequently show abnormalities which may be considered deviations rather than indicators of specific illnesses.

3. A psychiatric examination to rule out positive evidence of psychosis or of neurotic symptom-

atology. Frequently it may be found that the patient has a poor self-concept and a great fear of failure, and that he uses compensatory maneuvers to cover his non-adaptive behavior.

4. Psychological tests for organic disorders, e.g., the Bender-Gestalt test, the Wechsler Intelligence Scale for Children, Form Board tests.

5. A thorough review and complete assessment of the child's academic standing (tests in reading, arithmetic, abstract reasoning).

### Treatment Program

If an adequate treatment program is instituted, the prognosis can be fairly good: treatment has proved effective, for example, in overcoming visual-motor handicaps and in reducing emotional lability.

The following suggestions are offered for an ideal treatment program:

1. Provide total management of the medical and neurological condition. General behavioral symptoms may require administration of diphenhydantoin sodium, thioridazine or other phenothiazines, diphenhydramine hydrochloride, dextro-amphetamine sulfate, or chlordiazepoxide hydrochloride.

2. Make provision for a special classroom and teaching situation. New academic techniques are now being developed that give promise that they can help the child overcome perceptual handicaps.

3. Offer counseling by the physician or social case worker to help parents deal with distortions and misunderstandings concerning the disorder. Counseling also helps parents handle the family problems that inevitably arise with these children.

4. Provide psychotherapy for the child, if needed. At times there are primary emotional symptoms which need treatment, but more often secondary emotional reactions are present and require attention.

### Discussion

The label "brain-damaged child" confuses the issue because it oversimplifies a complex picture. Thus, from a clinical standpoint, it may be more accurate to diagnose "an organic factor" or a "component of brain-damage" as but one part of a total clinical picture.

The organic factor, in one degree or another, is not as infrequent as one might suppose. In a recent study of a series of cases at the Children's Clinic, Institute of Living, for example, an organic factor was part of the diagnosis in about 30 per cent of 112 consecutive admissions for psychiatric evaluation.

Of great concern to child psychiatrists and other professional persons who deal with brain-damaged



children and their families is the tendency for fads to develop based on unscientific notions about the disorder. This tendency may extend beyond the general public into professional ranks.

Misconceptions about brain injury are particularly troublesome in the school system and cause a number of problems. Teachers, for example, assuming that brain injury implies a definite organic lesion, may believe that the child so labelled has suffered a permanent and irreparable injury. Their anxieties are aroused, much as they were by a diagnosis of epilepsy before that disorder was properly understood. Thus teachers may approach the child with anxiety and sometimes with hostility, because the situation contains unknown, frustrating and threatening elements. If, through proper understanding of the disorder, educators can be helped to overcome their initial reaction to the condition, their anxieties may possibly be transformed into constructive action.

Another problem in the school system lies at a deeper level, tied to unconscious attitudes toward a "damaged" person. These attitudes stem from association of "brain damage" with death and destruction and are, therefore, accompanied by hopelessness and animosity. A teacher, reacting with irrational and inappropriate frustration and rage, may suppress his strong feelings or, even more unfortunate, he may act them out in his relationship to the pupil. In any event, there is little hope that such a teacher can be effective in helping the child to learn.

A third problem in school systems relates to the professional persons who advise educators on these matters; this problem can be more serious than the first two. Psychiatrists, psychologists, and experts in hearing, speech, and visual or perceptual handicaps may themselves use the term "brain-damaged child" uncritically, influenced perhaps by current faddism. These professionals may unwittingly encourage educators to apply the term indiscriminately.

Parents also harbor misunderstanding about the term brain-damage. Some who do not have a brain-damaged child may fear that they do. This fear may foster thinking that is almost delusional in nature, even when clinical investigation excludes the diagnosis. In other cases, on the other hand, when such a diagnosis is clinically confirmed some parents may become obsessed with the diagnosis itself and lose sight of the child's total problem. Unconsciously they assess the child's situation on much the same basis as the teachers and educators just described, associating the difficulty with death, destruction and irreparable defect.<sup>6</sup>

The parents of a brain-damaged child are likely to react in the same way as do parents of children

with other serious or chronic illnesses such as mental retardation, nephrosis or leukemia. Initially they may deny the fact or refuse to face it, or they may become hostile toward the person who presents the diagnosis. Later the parents begin to feel guilt about the possibility that they had a role in causing the disorder. With help, many parents are able to work through their feelings of guilt, accept the child's handicap realistically, and cooperate fully with a treatment program. If they do not work through these guilt feelings satisfactorily, however, they may go from specialist to specialist, from clinic to clinic, from hospital to hospital, seeking further tests and refinements, new diagnoses or more expert opinions. No matter how clear the diagnosis or how well it is explained to them, and no matter how efficient and effective the suggested therapeutic program, guilt feelings nonetheless drive these parents to continue their quest. The tragedy in these maneuvers, of course, is the waste of precious years which might better be spent in establishing and adhering to a teaching, rehabilitation and psychotherapeutic program for the child.

Parents need help with these problems. Physicians or other professionals, serving as interpreters, can explain the child's behavior, making the parents aware that his fluctuations in perception are beyond his control. This understanding may help them accept the child's limitations. Sometimes, when the situation is aggravated because of certain elements in the personality structure of one or the other parent, social casework or psychotherapy may help revise that parent's attitudes towards the child.

**Summary**

1. The diagnosis of the "brain-damaged child" is a behavioral diagnosis and is not made on an etiologic or pathologic-microscopic basis. The name has been given to an important clinical entity. Its cardinal symptoms are impulsiveness, distractibility and restlessness, but its manifestations may be more varied.

2. The diagnosis, which should be made by a team of experts, requires: detailed personal and family history, especially to uncover any history of insult to the brain; neurologic examination including electroencephalographic study; psychiatric screening; psychologic tests specifically to determine the possible presence of perceptual disorder and organic signs; and profile of academic achievement.

3. The ideal treatment program covers: management of the medical or neurological condition including medication for behavioral symptoms; a

complete educational program using specialized techniques for retraining and teaching; counseling of the parents to help them accept and understand the diagnosis; and, if necessary, psychotherapy for the individual child who has primary or secondary emotional disorders.

4. There is a tendency for teachers, other professionals and parents, to misconstrue and react negatively to a diagnosis of "brain-damaged child." The teacher may tend to view the child's capacities without hope, and his ability to help the child may thus be impaired. Parents may also react irrationally to the diagnosis, and unless they can be helped to deal with their own guilt feelings they may hamper the treatment program.

5. It is suggested that in describing this syndrome the physician use "organic factor" or "com-

ponent of brain damage" as a designation more appropriate than the label "brain-damaged child."

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### THE GOOD OLD DAYS

DAVID LITTMANN, M.D.

WEST ROXBURY, MASSACHUSETTS

It came to me, in times gone by,  
That nature often helped the cure,  
That doctors tried but not to hurt  
And drugs were mercifully weak.  
It's little help, these modern days,  
To urge restraint, to watch and wait.  
To stay the hot and eager hand  
With sharpened blade and two-edged drug.  
The patient's come with a disease,  
He must be healed tomorrow.

An intravenous drip kept running—  
One never knows when it's required;  
A nasogastric tube with suction  
And oxygen, by tent or mask;  
A monitor displays the rhythm  
And calls each beat with raucous chant;  
Blood pressures taken on the hour  
Ensure an interrupted sleep  
While digitalis glycosides  
Are pushed beyond toxicity.

And now to thwart what might occur—  
Thrombosis is an ugly thought;  
Dicumarol and heparin,  
Statistics show, prevent most ills  
Like thrombus of the coronary,  
Infarction of the heart and baldness,  
Angina pectoris and heartburn,  
Flatulence and morning nausea.  
And tests are made so many times  
That arms turn blue and blood runs thin.

When my time comes, no matter how,  
I plan to hide, deny and lie.  
I'll not complain, divulge a symptom,  
Betray a sign, confess a hurt.  
I'll not accept my brother's kidney,  
Or wear a heart of chimpanzee;  
I'll not be joined to wires and tubing,  
I'll not be tracheostomized.  
If this seems strange from a physician,  
It must be I'm not ready yet.

*Reprinted from The New England Journal of Medicine, November 25, 1965, with permission of the author and the editor.*



# Commitment Of Alcoholics

## An Approach To Treatment

William B. Terhune, M.D.

■ There is a little known provision for the hospital commitment of alcoholics for a period of up to a year, or long enough to accomplish lasting results. It is a simple Probate Court procedure, designed for chronically intemperate patients who cannot be persuaded to undertake treatment of their own accord, or who are unwilling to continue treatment long enough to be of real help in bringing the illness under control. Alcoholics who are sent to mental hospitals on short-term commitments almost always leave as soon as they feel better, long before any lasting, constructive results have been effected. It is impossible to detain them unless this legal tool is employed. The availability of General Statute, State of Connecticut, Chapter 304b, Section 17-155-G, corrects this situation and, when indicated, the physician should advise the use of this law and help the patient and family to arrive at this decision. If it happens they are not amenable, he can take matters into his own hands, abiding by the terms of the law as written. (Copy appended.)

For patients who undergo treatment *involuntarily*, six months is the shortest period in which satisfactory results may be expected; in many instances a year is essential. If an alcoholic will undertake treatment voluntarily, it is most desirable. If not, and his illness is a threat to himself or others, society has provided an opportunity for the doctor to assume the initial authority to set the wheels in motion to see that the patient does get the medical care he needs. When a patient imbibes pathologically over a period of time and refuses treatment, forcible commitment gives him a chance for recovery. It is humane, therefore, for the doctor and the family to make this decision for him. An alcoholic who renounces drinking and voluntarily accepts treatment in a competent psychiatric facility also needs months of intensive care and, most important, both need post-hospital follow-up for years.

Fifteen per cent of the population of the United States are either alcohol-dependent or are true alcoholics. This is a serious, malignant disease which, if allowed to continue, will become increasingly destructive to the individual's health, work, interpersonal relations and, more especially, to his

spirit. Without spirit man is truly an empty shell. The patient should be told that he can no more cure himself than he could treat a cancerous growth.

A firm, unequivocal diagnosis must be made; this should not be difficult for the manifestations of the true alcoholic are clearcut. The nature of the illness should be explained, emphasizing that it is an addictive compulsion with which the patient cannot deal himself. There is no soft approach in this unpleasant medical duty. The doctor must not pull any punches. Alcoholics are usually bullies, liars, wheedlers and nuisances; many physicians tend to avoid these patients and sidestep responsibility for dealing with them adequately. He may resent the diagnosis, and the family may resent it, but the direct, courageous physician can here play a role of the utmost importance.

Many people mistakenly believe that alcoholism is a matter of morals or character. All people are vulnerable—if one drinks enough liquor for a long enough time, one becomes addicted. Most of us can quote the aphorism, "THERE BUT FOR THE GRACE OF GOD GO I." Being a true addiction, both the reactions and attitudes of the patient are the conditioned result of the chemical effect of this drug (later complicated by psychological and sociological factors). These are initiated by and are characteristic of it. The addictive use of alcohol produces progressive deterioration physically, psychologically, socially, and spiritually, regardless of the basic character and morals of the individual. The majority of alcoholics are fine people when not handicapped by the symptoms and results of the disease. These people are caught in the alcohol trap, unable to help themselves, but find it difficult to admit this illness. Afraid to voluntarily get along without alcohol, they are eventually grateful when the doctor places them under treatment and gives them a chance to recover.

The pharmaceutical effects of alcohol cause otherwise fine people to lie, cheat, steal, deceive—anything to gratify their compulsion. Alcohol

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anesthetizes judgment, interferences with thinking and temporarily inactivates memory to the extent that the patient is not fully aware of what he does, thinks or says. In many instances alcohol produces temporary mental aberration, not due to psychodynamics, but to the chemical action of the drug. Alcoholics suffer from amnesia, compulsions, delusions, confabulations and projections—the latter paranoid in nature. From the doctor's standpoint, the true alcoholic is not sane. To paraphrase a term, he merely wears the "Mask of Sanity." Such a patient is not well, even when not actively under the influence of alcohol. Thinking processes are distorted, he lives in a maze of distorted compensations and sublimations, burdened with improbable excuses and armed with stupid, threatening devices. He lives in a never-never world of his own.

Within a few days after he stops drinking, the alcoholic mistakenly thinks he is well. He must be free of alcohol for at least six weeks after drinking before he can become normal physiologically, and it takes months of intensive treatment, without alcohol, for him to recover psychologically. Then he must learn to live wisely and carry on prophylactic measures, under medical supervision, for years.

Alcoholism is not, as commonly thought, the result of tension, escape mechanism, homosexuality or other psychological factors. It is a true drug addiction like other narcotics. Some people are more vulnerable to drug addiction than others. To repeat: any human being, given enough alcohol over a sufficient period of time, will become alcoholic. The illness often results from increasingly careless social drinking, carried to the point where addictive demands of the body are a natural consequence and compulsive drinking, complicated by anti-social acts and attitudes follow. When this happens, it may be explained away by the patient, family, and often the doctor on the basis of any one or more of the usual psychological strains common to every-day life. Every human being suffers from these strains, frustrations and conflicts, and yet the majority do not resort to drugs. The alcoholic usually attributes his drinking to psychological burdens that the majority of the world accept as inevitable. Most people, unhandicapped by alcohol, have a better chance of successfully working through these frustrations and problems. The alcoholic, unable to think logically, finds his life complicated and confused by the same problems. Some patients, and even doctors, think that if the emotional stresses can be solved, the alcoholic will be well. *Experience proves this is not true.*

Alcoholism is a danger not only to the patient, but to others. In addition to the many accidents caused by intemperate drinkers, a very large number commit suicide. This fact is usually hushed up

by the family and doctors. Thus, even though it takes quite a while for most people to die as a direct result of alcoholism, a considerable number come to their deaths sooner than expected! Nearly all could be saved by proper treatment.

Great care should be taken in choosing the psychiatric facility suitable to treat an alcoholic. These people deserve and should have much better treatment than available at present. Just locking them up in a hospital, talking to them a few times, allowing them to "pour out their troubles" on the basis that ventilation will make them well will effect neither temporary recovery nor produce lasting results. The successful treatment of the alcoholic requires excellent facilities; dedicated, competent and persistent physicians. Under such conditions, many are permanently cured. A few people, realizing how few such places exist, are trying to better the situation, but the alcoholic is truly the "Forgotten Sick Man" in American medicine. Alcoholism is purely a medical problem, and in a medical unit he should be treated.

Our society and culture encourages alcoholism. When doctors once tackle this medical problem seriously in a determined manner, the picture will quickly improve. It would be of inestimable help if every physician, when he does a physical checkup on his patients, would find out what their drinking habits are and to what extent their drinking is increasing. If the physician discovers a patient is in danger of becoming alcohol-dependent, he should assist him along lines of prevention.

To sum up: The alcoholic, suffering like other addicts from a malignant disease, does not willingly give up the drug unless convinced by necessity or strong motivation. This may be the threat of losing his job, spouse, children, or commitment for treatment. Short term treatment does not work on the addicted alcoholic. The purpose of this memorandum is to call to the attention of physicians the fact that when all other procedures fail, the Connecticut Legislature has provided a wise and humane measure to enable families to place such patients under enforced medical treatment for long enough to get results. Special care should be used in the choice of a psychiatric facility which is experienced in the intensive care necessary in these cases. Every patient should be followed up periodically for years.

The procedure for commitment is simple. A member of the family appears before a Judge of Probate, requesting commitment of the patient to a psychiatric facility. The patient is notified prior to the Hearing. It is desirable that both family and patient be represented by counsel at the Probate Court Hearing. The Judge appoints two physicians familiar with the patient's illness to testify that



they have examined him within the last few days; that to their knowledge the patient has been consistently under the influence of alcohol over a protracted period; that in their opinions the patient is now unable to help himself; that they therefore recommend hospitalization for a sufficient length of time to produce an expectation of lasting results. It is wise for the testifying physicians to write their reports, setting forth their observations and facts in support of the testimony. The Probate Court takes responsibility for such commitments, therefore the physicians are not liable for retaliatory suits. The doctors merely state the facts, submit a medical diagnosis and recommendations.

GENERAL STATUTES OF CONNECTICUT, CHAPTER 304b  
COMMITMENT OF ALCOHOLICS

Section 17-155g. Commitment procedure. When any person has become so addicted to the intemperate use of alcohol as to have lost the power of self-control, the court of probate for the district in which such person resides or, when his place of residence is out of the state or unknown, the court of probate for the district in which he is at the time of filing the complaint, except in cases where it is

otherwise expressly provided by law, shall, on application of the selectmen of the town where he resides or, when his place of residence is out of state or unknown, the selectmen of the town in which he is at the time of filing the complaint, or of any of his relatives, and after such reasonable notice to him as the court prescribes, make inquiry and if it finds him to be so addicted to the intemperate use of alcohol as to have lost the power of self-control, may order him to be taken to any private mental hospital or general hospital with psychiatric facilities in this state for treatment, care and custody for *not more than twelve months* if such hospital is able to accept such person and if he, or any person or persons liable for his support, will pay the charges for his treatment and cure therein. The probate court shall not make such order without the certificate, under oath, of at least two practicing physicians, given after a personal examination, made within one week before the time of such application or commitment, that, in their opinion, such person has become so addicted to intemperate use of alcohol as to have lost the power of self-control and ought to be placed in a hospital authorized to accept and treat such persons.

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# Wounds Of The Upper Extremity: Use Of Grafts And Flaps

Marvin S. Arons, M.D., D.M.D.

## Introduction

■ The surgical treatment of upper limb wounds should be correlated with the type and extent of injury, the character of the wound, the injury-treatment interval, the age and sex of the patient, and the dominant hand. Discussion will be limited to injury of the hand and forearm in which there is an actual loss of or irreparable damage to the skin and subcutaneous tissue due to trauma other than burns. Because of the many variables involved, digital injuries also have been omitted. In the experience of many, most upper extremity skin-loss wounds with the exception of burns, have been due to vehicular accidents and gunshots.<sup>1</sup>

## The Acute Injury

When the wound is a simple avulsion of skin without exposure of underlying tendons, bone, or nerves, the management at two days post-injury might be the same as it would have been at two hours: cleansing and debridement followed by split-thickness skin graft coverage. Conversely, the crushing wound should not be considered a fresh injury even at twelve hours.<sup>2</sup> Therefore, time limits are not absolute.

Although small wounds without evidence of damage to underlying structures on physical examination and X-ray can be repaired under local anesthesia, regional block or general anesthesia is usually preferred. A pneumatic tourniquet should be placed on the arm in readiness so that it may be used as necessary to achieve a dry field during irrigation, exploration, and debridement of the wound. Avulsed, contused, and deeply abraded skin must be evaluated closely for viability in a non-bloodless field. As a general rule when skin and soft tissues of the upper extremity have questionable viability, they should be excised and discarded (Fig. 1). This would include areas of dusky skin, avulsed flaps with narrow distally based pedicles, flaps with diminished reactive hyperemia, and edges of wounds that do not freely bleed. Of course, gentle meticulous surgery combined with sharp dissection and hemostasis is essential. Normal skin is even discarded when necessary so that the borders of the wound will fall in the proper lines of tension and not produce a post-operative scar contracture. One cardinal rule in hand surgery is to obtain a



FIGURE 1

Gunshot wound of volar surface of forearm. Note fragmented tissues requiring debridement.

closed wound as soon as possible to prevent infection, fibrosis, and secondary deformity.

## Wound Closure

Small avulsion wounds can be closed by simple primary suture. However, one should not close wounds of this type under tension and the use of local flaps for closure (as in wounds of the lower extremity) has been limited to a few very well selected cases.<sup>1</sup> The upper extremity has little skin and soft tissue to spare for such plastic surgery maneuvers although finger injuries constitute an exception to this rule and cross-finger flaps can be utilized. When primary closure is not possible without tension and when deep structures are not exposed, the best technique is to apply a split-thickness skin graft to the wound (Fig. 2). Depending upon the sex and occupation of the patient, the skin graft can be taken from the ipsilateral or contralateral arm or forearm or from the bathing suit (or bikini) area. Use of the thigh as a donor site

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should be avoided since it can interfere with ambulation. The use of such a free split-thickness skin graft will produce more optimal results than by using excised avulsed flaps as free full-thickness skin grafts.<sup>1, 3, 4</sup> Grafts to such wounds of the upper extremity are usually not left exposed but are sutured on with a stent dressing and then a bulky occlusive-compressive dressing is applied with an adhesive tape sling which can suspend the limb during the post-operative period. If primary closure by suture or by graft is inadvisable initially, then just a compression dressing should be applied. Such circumstances could arise when: 1) complete hemostasis was not obtainable, 2) a wound overly impregnated with foreign bodies could be debrided only with extreme difficulty and 3) a patient is in critical condition from other associated injuries. In these cases, the wound can then be closed secondarily with sutures or skin grafts (Fig. 2) two to four days later (or even a pedicle flap if indicated).

#### Pedicle Flaps

In avulsion wounds with exposed bone, open joints, divided nerves, or divided and/or denuded tendons, the growth of free grafts will not be supported and will necessitate the use of a direct distant pedicle flap to preserve these structures. The introduction of flap tissue offers skin coverage that is able to survive independently of the bed or structures it protects. In addition, flaps improve the circulation of the part and provide a surface under which subsequent reconstruction may be undertaken. Furthermore, this method of skin replacement restores many of the protective qualities of normal skin which are essential to reconstruction. Flaps will give a result unattainable by free grafts in such conditions and will preserve the function of the underlying anatomic structures.<sup>1, 2, 3, 4, 5, 6, 7</sup>

Flap grafts from the trunk to the upper extremity usually originate between the nipple line and the pubis and the mid-lateral or mid-axillary lines. The selection of the pedicle site should depend upon the location, size, and nature of the recipient defect, ease of application, patient comfort, availability of skin, and cosmesis.<sup>8</sup> All pedicles to the upper extremity should be closed either by tubing (Fig. 3) or by split-thickness skin grafting to avoid the undesirable effect of an open wound contributing to local induration and fibrosis. If cross-chest pedicles are not preferred, then lower abdominal flaps are indicated. In most instances, pedicle flaps of a length-width ratio less than 2 : 1 can be raised and transferred without previous delay (Fig. 4). Beyond this ratio, the flaps should be delayed and the wound of the upper extremity surgically dressed in one way or the other in the meantime

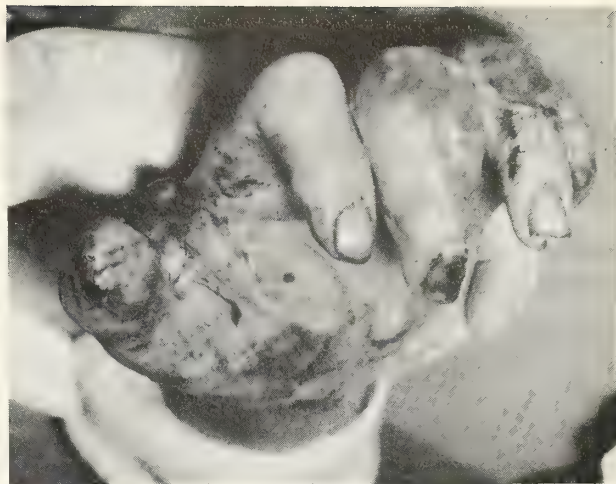


FIGURE II

Blast injury of the hand with loss of thenar space and soft tissues on dorsum of long and ring fingers. Split-thickness skin grafts applied three days post-debridement.

(Fig. 5).<sup>1</sup> The long axis of the flap should never cross the mid-line of the trunk and it also would be inadvisable to base a flap at or near the mid-line. The first step in determining the site to be used for flap coverage is to use a pattern on the trunk

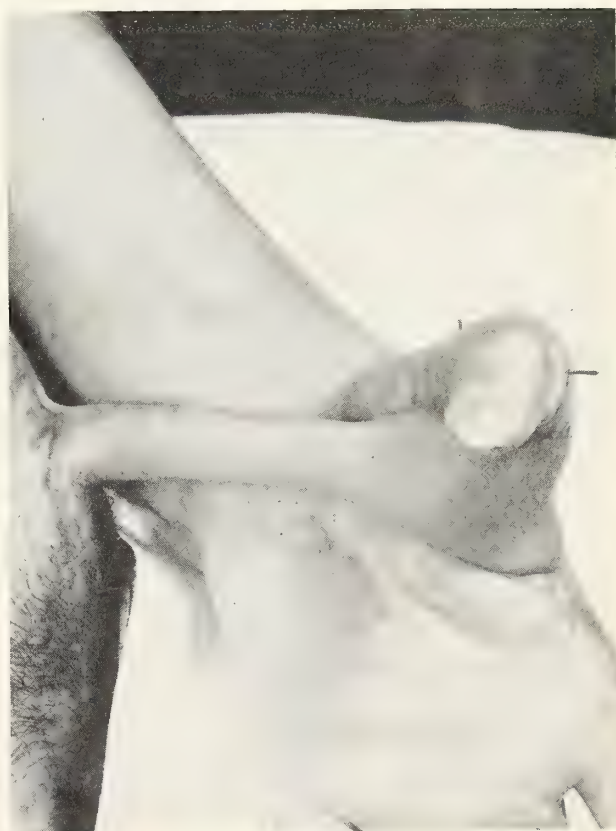


FIGURE III

Thenar space undergoing reconstruction with inguinally based abdominal tube pedicle (see Fig. II).

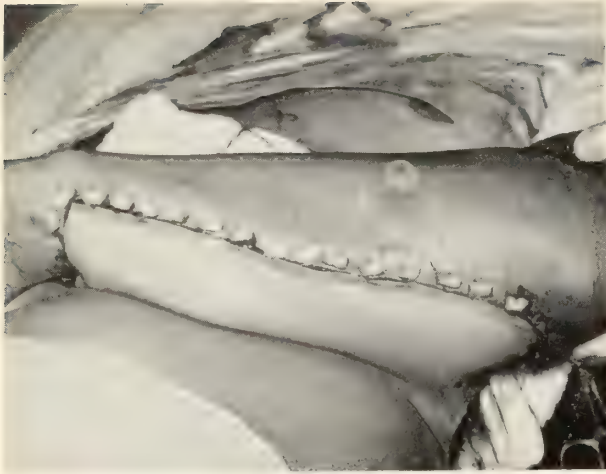


FIGURE IV

Direct inferiorly based abdominal flap applied to wound after thorough debridement. Note the wire-bolster sutures (see Fig. I).

with the involved or uninvolved extremity. Joint position, projection of post-operative patient comfort, and determination of relaxation of the prospective flap when attached are factors that must be considered. Semi-circular flaps should be avoided because of the tendency to develop a "biscuit deformity" when the scar contracts. This is the reason that the design of the flap should always be rectangular (Fig. 5). In order to avoid trauma to the edges of the flap, it is sutured into its recipient area with 3/4 vertical mattress sutures of No. 36 stainless steel wire tied over a moist cotton bolster on the non-flap side of the suture line (Fig. 4).<sup>9</sup> This suture technique causes minimal disturbance of the external skin surface and edge of the flap.

Elastoplast, supplemented by adhesive tape and padding, is used for immobilization (Fig. 5). Plaster fixation has been found cumbersome for the patient, laborious for the surgeon, and unnecessary in most cases. The flap itself should always be left completely exposed to allow direct observation. Ambulation may be permitted several days post-operatively. The majority of these flaps can be severed and inset about three to four weeks post-operatively. More often than not however, a delay incision is made in the pedicle, that is, the base of the flap is only partially detached from the trunk. Approximately one week later, the flap is completely detached and sutured into place.

### Summary

1. *Split-thickness Skin Grafts:* Split-skin grafting is one of the most frequently used methods of obtaining primary closure of the wound and healing when there is loss of surface tissue. A split graft can take over any viable tissue except open joints,



FIGURE V

Due to length-width ratio, delay incisions were required for this abdominal flap. Note its rectangular design.

bone denuded of periosteum and tendon denuded of paratenon. It may serve as permanent cover or preserve hand tissues for later reconstruction. Also, skin grafting is less demanding of surgical technique.

2. *Full-thickness Skin Grafts:* In elective hand surgery these grafts have application but have little place in the management of the acute hand injury.<sup>1, 3</sup> These grafts require an ideal recipient bed for survival. When combined with Z-plasties, they are useful to relieve palmar contractures of the digits.<sup>10</sup>

3. *Fillet Skin Grafts:* When skin is available on the digits or other surfaces on which the functional architecture is irreparably damaged, this skin may be used to resurface defects in which it is desirable to maintain the special qualities that the hand skin possesses. This implies salvaging skin with its nerve and blood supply intact and finds its greatest application in secondary or elective reconstruction of the hand and would include the neurovascular island flap.<sup>3, 6</sup>

4. *Cross-finger Flaps:* These flaps provide a useful solution for cutaneous defects of the digits on which local skin and subcutaneous tissue is desirable (as with exposed flexor tendons).

5. *Pedicle Flaps:* These furnish good soft tissue coverage with a protective dermal pad and relax all tissues within the hand or forearm thus improving nutrition and bringing in new circulation. When not applied directly to avulsed or denuded areas they may be delayed and later set-in to cover any wound from days to weeks after the injury provided that the wound is clean. As soon as their nerve supply returns, these flaps will stand the wear and tear of rough use and furnish a bed under which





FIGURE VI

Complete range of flexion and extension of fingers seen on double-exposure taken four months after division and set-in of flap seen in Fig. IV.

tendons can glide (Fig. 6). Flaps do not shrink but they can grow and gain weight with the individual. Skin which has been properly transplanted by use of the pedicle should lie flat without excessive subcutaneous tissue and with borders that are inconspicuous and which do not interfere with flexion creases (Fig. 7). Although operations on deeper



FIGURE VII

Reconstruction of contracted thenar space completed. Note restoration of power grip (see Figs. II and III).



FIGURE VIII

Same patient in Fig. V after resurfacing 150° of forearm with abdominal flap. Dynamic splint being utilized prior to nerve and tendon surgery.

structures of the extremity may be done simultaneously with a pedicle graft and time is saved in this manner, elaborate reconstructions should not be attempted<sup>8</sup> (Fig. 8).

(All cases from the Plastic Surgery Division, University of Texas Medical Branch, Galveston.)

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# The Contributions Of The Horse To Knowledge Of The Heart And Circulation

## IV. James Hope And The Heart Sounds

J. D. McCrady, D.V.M., H. E. Hoff, M.D., and L. A. Geddes, Ph.D.

### Introduction

■ One of the high points in French clinical medicine was the discovery of mediate auscultation by Laennec, whose classical report first appeared in 1819; an English edition soon followed in 1821.<sup>1</sup> The importance of the new method, auscultation, and of the new tool, the stethoscope, which Laennec invented and which made routine auscultation possible, was quickly appreciated. In a few years a whole army of young physicians, trained under Laennec, began to return to hospitals throughout the world, bringing their expertise in the new technique with which to challenge the older methods of their seniors. They were sure of themselves, eager to show their prowess, and they were often disturbingly right in the insights the new method provided. Like other bearers of new ideas, they were not always welcomed with any eagerness, but in the long run they established auscultation as one of the major techniques in medicine.

One of these young men was James Hope. After taking his medical degree at Edinburgh in 1825 he migrated to St. Bartholomew's Hospital in London where he became a Diplomat of the Royal College of Surgeons in 1826, and set off for the Continent for two years. His experiences in Laennec's clinic at the Charité were decisive; he became an expert in auscultation, and returning to London in 1828, he made it the cornerstone of his success as a physician. If he was a young man in a hurry there was reason for it; he was afflicted with pulmonary tuberculosis brought on by overwork in the wards and clinics of St. Georges Hospital, and by the fatigues of a practice that continued to grow even when he was partially invalided. The whole span of his productive life was from 1828 to 1841, when he succumbed to the disease.<sup>2</sup> During this brief time he published, in 1832, 1835 and 1839, three editions of his great *Treatise on the Diseases of the Heart and the Great Vessels*.

*Supported by Grant HTS 5125, National Heart Institute, National Institutes of Health, Washington, D. C. From the Department of Physiology, Baylor University College of Medicine, Texas Medical Center, Houston, Texas.*

### The Nature Of The Heart Sounds

One of Laennec's legacies concerned the nature of the heart sounds. Not at his best when he wrote on the subject, Laennec considered the first sound, dull though distinct, to be a reflection of ventricular systole, but he attributed the second sound, "a noise resembling a valve, or a whip, or the lapping of a dog" to the contraction of the auricles, forgetting or neglecting Harvey's careful analysis of the rapid sequence of contraction of auricles and ventricles preceding the longer diastolic pause.

Harvey had himself written about the heart sounds in *de Motu Cordis*, when he compared the sequence of cardiac contractions to the process of swallowing, concluding that "It is easy to see when a horse drinks that water is drawn in and passed to the stomach with each gulp, the movement making a sound, and the pulsation may be heard and felt. So it is with each movement of the heart when a portion of the blood is transferred from the veins to the arteries, that a pulse is made which may be heard in the chest."<sup>3</sup> Whether he ever distinguished the two heart sounds is purely a matter of conjecture, but we know that in notes for his lectures in 1615 he wrote in Latin, "W. H. demonstrates by the structure of the heart that blood is continually being transferred through the lungs into the aorta," concluding in English, "as by the clacks of a water bellows used to raise water."<sup>4</sup> Figure I illustrates the ancient method of using bellows to raise water with which Harvey was familiar. Is it too much to

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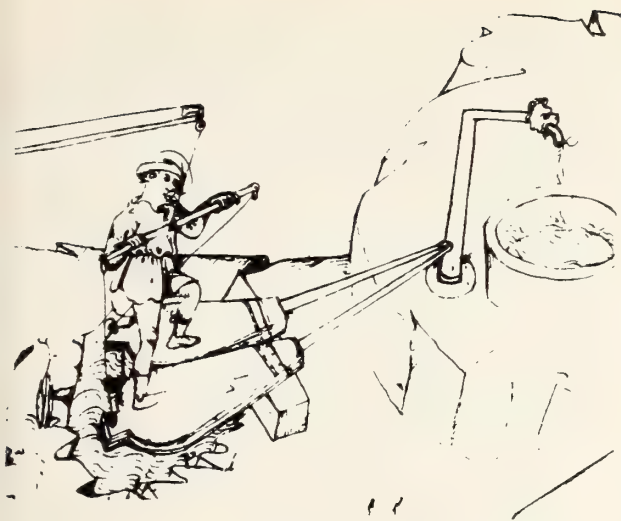


FIGURE I

"As by the clacks of a water bellows used to rayse water." The word "clacks" has both the meaning of "valves" and "sounds," the first deriving from the second. It is possible that Harvey shifted from Latin to English at this point just so that he could use this word, with its double meaning and its implication of a sound and its valvular origin. It is not unlikely that Harvey's acquaintance with pumps of this kind was part of the background out of which he developed the idea of the circulation, for the notion of the heart as a pump is one of its central concepts.

The contrivance pictured here is from the Jacobus Marianus manuscript (Munich) and dates from 1430. The arrangement of two bellows makes it possible to maintain a constant outflow without an air chamber. Each bellows would require both inflow and outflow valves, and would give a double sound with each stroke. The yoke supported at its center takes care of filling; as one bellows is pushed down, the other bellows is pulled up by the rope attached to the end of the yoke.

suggest that he had heard the two separate sounds and located their origin in the sequential closure of A-V and aortic valves?

Here was a subject for experimental analysis, and in 1830 Hope began a systematic study of the problem<sup>5-8</sup> asking himself the following questions:

1. Do the auricles contract immediately before the ventricles?
2. Does an interval occur between the two contractions, or is the succession so rapid as to amount to continuity of action?
3. Does the ventricular contraction cause the impulse, pulse and first sound?
4. Do the ventricles contract completely, and do they remain closed and empty, during the interval of repose? Or—
5. Do the ventricles dilate again immediately after their systole: and is this dilatation attended with an influx of blood from the auricles?

6. Is the influx of blood into the ventricles during their diastole the cause of the second sound? If not—
7. What is the cause of the second sound?

His first experiment was performed at the establishment in Oxford Street, of Mr. John Fields, a veterinary surgeon, and was described as follows:

"Experiment 1.—An ass, of which the pulse and impulse were forty-eight per minute, was instantaneously deprived of sensation and motion by a smart blow on the head. The trachea was opened, a large bellows-pipe introduced, and artificial respiration maintained; while, at the same time, the left ribs were sawn through near the sternum, and forcibly bent back and broken, so as widely and completely to expose the heart immediately behind the left shoulder: the whole was accomplished in less than five minutes.

"The pericardium was next opened, and the auricles and ventricles fully displayed. The action of the heart was at first quick, tumultuous, quivering, and irregular; but after the lapse of about three or four minutes, it became regular and slower. The auricle was now seen to contract *first*, and the ventricle instantly afterwards; or, in more descriptive language, a slight contractile motion, accompanied with very inconsiderable diminution of volume, was observed to commence in the auricle, and to be propagated rapidly to the ventricle. It was not, however, so quick that it could not easily be followed by the eye; yet it seemed to be rather a continuity of action, than to consist of two consecutive parts.

"The ventricular contraction appeared, and was felt by the hand to consist of a sudden energetic jerk, accompanied with a depression of the centre or body of the ventricle. This contraction was heard (through the stethoscope, applied *immediately* to the organ) to be accompanied by the ventricular sound. A note was accordingly dictated, that, 1. *The ventricular sound was heard whilst the ventricle was seen to contract.* At an interval of time equal to that which intervenes between the first and second sounds of the heart, the contraction was followed by a sudden, jerking re-expansion or diastole, which appeared *to elevate the body of the ventricle more than the previous contraction.* Hence one of the party (Mr. Lane) expressed his opinion that it was the *diastole*, and not the systole, that occasioned the impulse. This opinion rendered it necessary instantly to repeat all our observations. The stethoscope was accordingly resumed, and several times applied by Mr. Field and the writer alternately, each counted 1, 2, synchronously with the sounds which he heard, and the impulse communicated to his ear; while others applied their hands to the ventricle, and at the same time in-

spected its motion. It was now proved, to the perfect satisfaction of Mr. Lane and all present, that the sound 1, and the impulse felt by the auscultator, coincided with the *visible* depression (i.e. contraction) of the ventricle, and the impulse felt by the hand. It was therefore dictated that, 2. When the action of the heart was become slower, (*supposed to be about forty per minute*), and was becoming feeble, the ventricular systolic sound and the impulse were heard, seen, and felt, both by the ear and hand, to be simultaneous.

"At an early part of the experiment it had been unanimously agreed that the ventricle never contracted fully, though it was then acting with great power. It was, therefore, dictated, that, 3. *The ventricular never contracted fully.*

4. It remained apparently full during the intervals of repose (i.e. from the conclusion of the diastole to the commencement of the next ventricular contraction).

"On interposing the hand between the apex of the heart and the rib, which had been left above that part, the fingers were struck vigorously by the apex of the ventricle during its systole, at the moment that its body was in the act of retraction.

"As the action of the heart, after ceasing to be tumultuous, became somewhat feeble, the second sound was never very audible. It was distinctly heard, however, by Mr. Field and the writer; but as the others could not satisfactorily recognize it, a general note was deemed inadmissible, and a by-note only was dictated, the point being reserved for further investigation at the next experiment."

The conclusions drawn from this and a second similar experiment were, that

- "1. The auricles contract so immediately before the ventricles, that the one motion is propagated into the other, almost as if by continuity of action; yet the motion is not so quick that it cannot readily be traced with the eye.
- "2. The extent of the auricular contraction is very inconsiderable, probably not amounting to one-third of its volume. Hence the quality of blood expelled by it into the ventricle, is much less than its capacity would indicate.
- "3. The ventricular contraction is the cause of the impulse against the side; first, because the auricular contraction is too inconsiderable to be capable of producing it; second, because the impulse occurs after the auricular contraction, and simultaneously with the ventricular, as ascertained by the sight and touch; third, because the impulse coincides so accurately with the pulse in arteries near the heart, as not to admit of being ascribed to any but the same cause.

- "4. It is the apex of the heart which strikes the ribs.
- "5. The ventricular contraction commences suddenly, but it is prolonged until an instant before the second sound.
- "6. The ventricles do not appear ever to empty themselves completely.
- "7. The systole is followed by a diastole, which is an instantaneous motion, accompanied with an influx of blood from the auricles, by which the ventricles re-expand, but the apex collapses and retires from the side.
- "8. After the diastole, the ventricles remain quiescent, and in a state of apparently natural fullness without distention, until again stimulated by the succeeding auricular contraction.
- "9. The *first sound* is caused by the systole of the ventricles.
- "10. The *second sound* is occasioned by the diastole of the ventricles."

A second series of experiments begun on Aug. 10, 1831 at which three more asses were studied in the same way, and was concerned especially with the second sound, as follows:

"3) with what motion of what part does the second sound coincide, and what is its cause? Is it the ventricular diastole?

- A. The second sound coincides with a motion, sensible to the touch and sight, by which the ventricle returned from its systole to the same state, with respect to size, form, and position, as before the systole. This motion was relaxation or diastole."

"The second sound or that of the ventricular diastole, is generated by a more simple mechanism, and is, consequently, more uniform in its character. When the diastole takes place, the blood, put in motion by a number of concurrent circumstances already particularized, starts with instantaneous velocity from the auricles into the ventricles, and the reaction of the ventricular walls on its parieties, when their course is abruptly arrested by the completion of the diastole, is, I conceive, the cause of the loud, brief, and clear sound."

This concept of the second sound did not meet general approval, and in Paris, Rouanet, writing his medical thesis,<sup>9</sup> returned to the valvular theory that Harvey himself may have had in mind. Connecting an excised aorta with its valves to a long glass tube filled with water, he alternately compressed and relaxed a bladder partially filled with water, attached below the valves, and produced a sound each time the valves came together as he relaxed his compression of the bladder. Thus challenged, Hope performed a final series of experiments, again on the ass, aimed at working out the following Propositions:



- "1. Is the second sound loudest over the sigmoids, and is it so *near* to seem produced immediately under the stethoscope?
  - "2. Is the first sound loudest over the two auricular valves respectively; and is it so *near* as to seem produced immediately under the stethoscope?
  - "3. Place the origins of the aorta and pulmonary artery between the finger and thumb; apply the stethoscope on the heart near the sigmoids; instantly after the ventricular systole, close the arteries, so as to prevent the reflux of the blood and consequent expansion of the valves, and see whether this annihilates the second sound.
  - "4. Relax the fingers during the interval of repose, and see whether this reproduces the second sound at its wrong interval.
  - "5. Push the knuckle, or the auricle, into each auriculo-ventricular orifice, so as to prevent the expansion of the auricular valves, and see whether this annihilates the first sound.
  - "6. Introduce a bent needle into the aorta, and hold open one or more of the semilunar valves, so as to permit free regurgitation. Notice whether this occasions a murmur with the second sound. The pressure of the aortic system being thus thrown on the ventricle, will it close the mitral valves? See whether this annihilates the first sound on that side."
- The experiments themselves, carried out again at Mr. Field's veterinary establishment, proved without any further doubt the valvular nature of the second sound:
- "Obs. 10. Before the pericardium was opened, *both* sounds were very distinctly heard.
- "11. Both were also distinctly heard through the lung interposed between the heart and the end of the stethoscope.
  - "12. About two or three inches up the aorta from its origin, the second sound was heard (but not the first), alternating with the impulse as felt by myself (not by Mr. Keate), in consequence of my having previously noticed the same in the living subject, as stated at p. 27).
  - "13. The second sound was decidedly more distinct over the origins of the aorta and pulmonary artery than on the body of the ventricles; and, in that situation it was louder than the first sound at the same point. It had exactly its natural short, clear, flapping character.
  - "14. The aorta and pulmonary artery being compressed between the fingers, the first sound was accompanied with a loud murmur, and the second was stopped.

- "15. A common dissecting hook was passed into the pulmonary artery, so as to prevent the closure of the semilunar valves: the second sound was impaired, and a hissing murmur accompanied it. A hook was passed into the aorta, so as to act in the same way on the aortic valves: the second sound entirely ceased, and was replaced by a prolonged hissing. (Heard by several.)
- "16. When the hooks were withdrawn, the second sound returned and the hissing ceased."

It would be pleasant to relate the unalloyed satisfaction that publication of these data, so fundamental to the whole practice of auscultation, should have brought the author. This was not to be. C. J. B. Williams, who had completed his medical training in Edinburgh a year before Hope and had also attended Laennec's clinic at the Charité, had himself published a volume on auscultation that went through many editions,<sup>10-12</sup> published the results of the 1834 experiments, which can be seen, were crucial to the understanding of the second sound. In the third edition of his book, which also appeared in 1835, he claimed the results for his own. There is no doubt that Williams did participate in the experiments of 1834, and did retain a copy of the Propositions and the results of the experiments. They were clearly couched in the same orderly fashion that Hope had established in 1830 and employed subsequently; they were unmistakably Hope's. Williams however claimed that he had invited Hope to participate in the final series of experiments and had been responsible for the experimental protocol, which Hope then authored. The controversy was never settled; it seems obviously to have been mismanaged by Sir Benjamin Brodie, who was asked to arbitrate it, and Hope's early death made it impossible to compose the differences between the two antagonists.<sup>13-15</sup> It will probably never be possible to settle the matter definitively, though the entire sequence of events, starting with the experiments of 1830 and 1831, on the ass, at Mr. Field's establishment and culminating in 1834, suggests that the same person was author of the whole. This could only have been Hope.

### **Repetition Of Hope's Experiment**

The experiments carried out by the authors were performed on a ten-year old jackass weighing 175 kg. It was pre-medicated with morphine sulphate (10 mg. per kg.) and anesthetized with a proprietary veterinary anesthetic\* consisting of a mixture of chloral hydrate, pentobarbital and magnesium sulfate, given as required to maintain surgical anesthesia.

\* Equithesin, Jensen-Salsberg, Kansas City, Missouri.

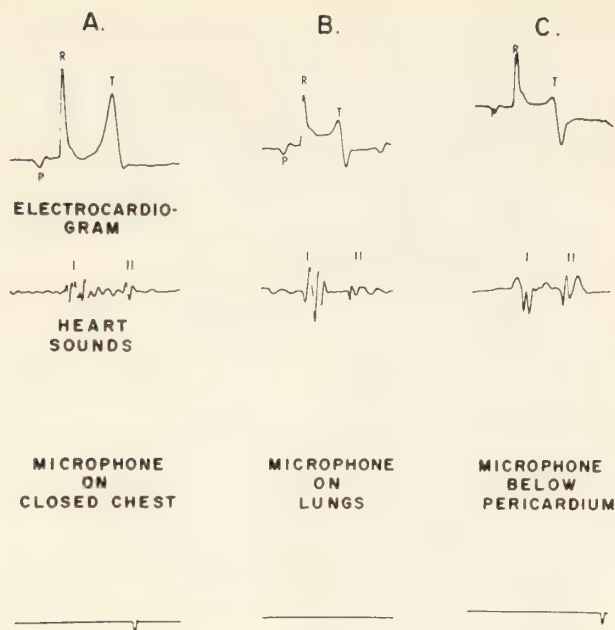


FIGURE II

This illustrates the presence of heart sounds when recorded across the chest wall (a), across the lungs after the chest wall has been removed (b), and between the heart and the pericardium (c), reproducing Hope's evidence that the heart sounds are intrinsic, and not caused by impact of the contracting or dilating heart against the chest wall.

Figure IIa shows in the top channel a typical equine electrocardiogram as recorded from lead II, with its inverted P wave and large T, while below are recorded the heart sounds as picked up by a contact microphone placed on the left chest over the third interspace near the anterior costochondral junction, where the maximum sounds were heard. The first sound, which begins somewhat after the onset of the R wave, is typically longer in duration than the second sound which is correlated with the end of the T wave. Figure IIb was recorded after removal of 6 inch segments of the left third and fourth ribs beginning at the anterior costochondral junction, to expose the heart. The lungs were inflated by artificial respiration and the microphone was permitted to float upon the inflated lung. In IIc the microphone was inserted between the pericardium and the heart. Despite the absence of the anterior chest wall the sounds appear normally, disposing of suggestions that they were related to the apex beat or other mechanical collision between the heart and the chest wall.

A specially designed spreader was then introduced into the aorta and its tip directed downward between the cusps of the aortic valves. The handle was then rotated, spreading the leaves of the instrument and preventing the closure of the aortic valves. As this took place the second heart sound,

which had been present (IIIa), disappeared (IIIb), only to reappear as the instrument was closed and the valves were permitted to open and close normally (IIIc). Figure IIIb does indeed show a small vibration and it is likely that this represents the contribution made by the closure of the valves of the pulmonary artery, the operation of which was not altered by this procedure.

### Conclusion

We need to remind ourselves that the experiments of Hope were performed before Ludwig had introduced graphic recording in Physiology, before Chauveau and Marey had applied it to the analysis of the events of the cardiac cycle, and long before heart sounds were ever recorded by the graphic method. Hope had only his stethoscope, and relied on the testimony of a number of witnesses to confirm the results of his experiments. The use of a large animal was probably the critical factor in Hope's success, for with smaller animals the sequence of beats is so rapid that it becomes virtually impossible to identify the sounds arising from each cycle, and to correctly place them in the cardiac cycle. Figure VI, made from an anesthetized dog illustrates three of the four heart sounds and places them in their position in the cardiac cycle.

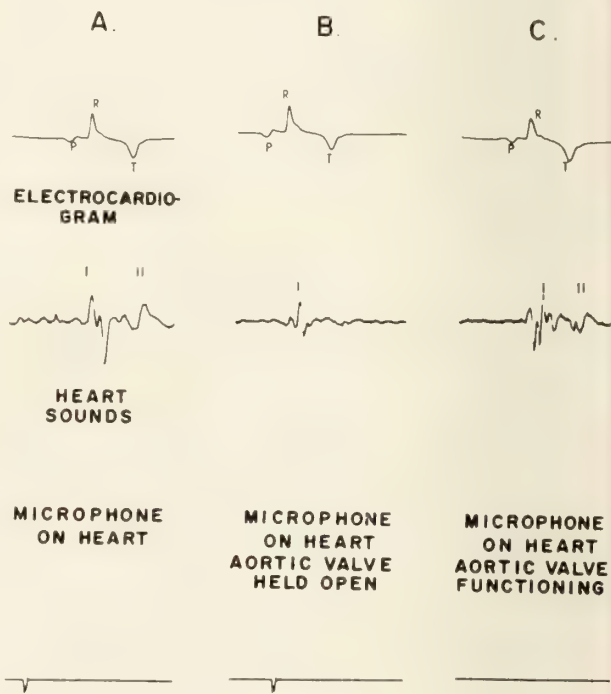


FIGURE III

This illustrates Hope's classical experiment of preventing the closure of the aortic valves to suppress the second heart sound, and thus to demonstrate its causation by the closure of these valves in early diastole. In a, the spreader is in place but unopened. In b, the valves are held open and the second sound disappears. In c, the spreader is again closed and the valves close normally and the second sound reappears.



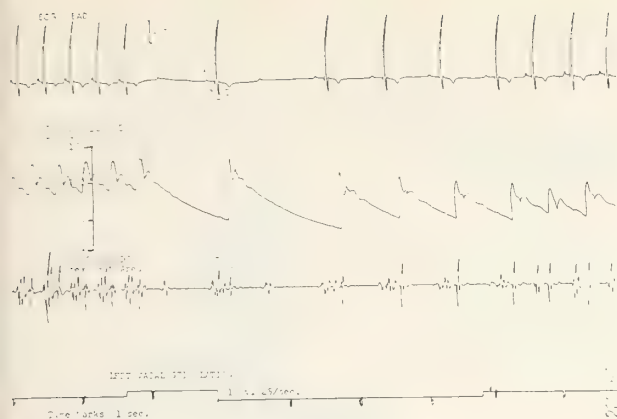


FIGURE IV

This figure illustrates the difficulty that everyone must have encountered in analyzing the heart sounds in the rapid heart of small mammals before graphic recording. At the left the ECG, blood pressure and heart sounds are seen at the usual rapid rate of an anesthetized dog, and it is easy to understand how the various sounds might be confused if they were only heard and not recorded with the other events. When the heart is slowed by vagal stimulation, a technique unknown to Hope and his contemporaries, the two sounds stand out clearly and are easily identified. The occurrence of partial block, with two isolated atrial systoles reveals the atrial or fourth sound that ordinarily combines with and is obscured by the first sound.

Although the two major heart sounds are today universally described as lubb-dup, the date of the origin of this term is by no means certain, although the following appears to clearly identify the author of the term.

In "A Rational Exposition of the Physical Signs of Diseases of the Lungs and Pleura"<sup>10</sup> (1828), Williams described the first and second heart sounds as "Dull, slow noise, immediately followed by a short quick one to which succeeds a short interval of silence." In Williams' subsequent text, "The Pathology and Diagnosis of the Chest" (1835), there is no evidence of the term "lubb-dup." However, in Williams' fourth edition of "The Pathology and Diagnosis of Diseases of the Chest"<sup>16</sup> (1840) he wrote "If we listen either with the stethoscope or the ear alone applied to the region of the heart, we hear at each pulse two sounds following each other in quick succession, and succeeded by an interval of silence until the next pulsation. The first is a long rather dull sound, the second is a short abrupt flap. Some French writers have used a very wrong-sounding word for this double sound, by calling it "tic-tac." If it is to be given at all by the symbols of articulate sounds, the word "lubb-dup" will best express it." By 1874 Dunglison,<sup>17</sup> in his dictionary of that year wrote, "Dr. C. J. B. Williams suggests the word lubb-dup

as conveying the notion of the two sounds." Thus there can be little doubt concerning the origin and the author of the term lubb-dup.

Even with all the assistance that the techniques of experimental medicine afford today in the way of anesthesia, artificial respiration, adequate surgical instruments, and a panoply of recording devices, the experiment is not easily performed on such a large animal. To have conceived it and carried it out with success a hundred and thirty years ago was no small achievement, and it is not difficult to understand why Hope's name has come down to us as one of the great names in cardiology.

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(This is the fourth of a series of four articles.)

# THE PRESIDENT'S PAGE

## GUEST EDITORIAL

**B**ECAUSE of the interest in the work of the Connecticut Society for Medical Research, Incorporated, its Secretary, Doctor Michael Hume has kindly accepted my invitation to write the following article for this issue of the President's Page.

JAMES R. CULLEN, M.D.

### **Is Government Regulation Of Medical Research Necessary?**

We continue to see literature received in the mail and sometimes editorials, such as the one in the *New York Times* on November 28, 1965, charging that government regulation of medical research is necessary to prevent cruelty to animals. Doubtless, one's best instincts always will react violently to a charge of cruelty; but in fact, what is the situation today in medical research and how is the physician personally involved?

Our professional work has its scientific basis in medical research, and the unsolved problems that we face daily in patient care can be expected to yield in the future to new solutions as the scope of medical research broadens rapidly. Philosophically, we are involved too, because we place the highest value on human welfare and accordingly hold that such research is proper, including the use of animals where necessary.

Our commitment should go a bit farther than this I believe. In Connecticut, we are fortunate to have excellent laboratory animal care legislation, which was enacted in 1963 with the help of enlightened public opinion. The system of laboratory inspection now operating under this act belies the charges of cruelty and is a model for other states and the federal government. (Several bills now before Congress, such as HR 10049, purport to prevent cruelty. They are based on the erroneous assumption (1) that a significant number of biological scientists are now treating laboratory animals in inhumane ways, and (2) that licensing and inspection by the federal government would bring about a decrease in inhumane treatment.) We have an excellent organization, the Connecticut Society for Medical Research, which operates an educational program to increase public understanding of the aims, methods and achievements of medical research. We should support this work, particularly by our membership as individuals. Details can be found in the correspondence section of this issue on page 141. Better public understanding is a must these days to promote the best possible climate for medical research here and throughout the nation.

MICHAEL HUME, M.D.



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In addition to the above, members up to age 40 may now purchase their Accident and Health protection at a 25% reduction in cost.

Through its continued official sponsorship of our Group Plans, The Connecticut State Medical Society has once again made it possible to offer broadened coverage under these two time-tested policies to members of the Society. If you are not now enrolled, do not turn your back on old friends who have served Connecticut physicians for over a quarter of a century. If a sufficient number of new applications are submitted for the Major Medical Expense Plan, all policies will be issued regardless of past medical history. For full information write or phone.

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## A SPECIAL MESSAGE FROM THE CONNECTICUT MEDICAL POLITICAL ACTION COMMITTEE (COMPAC)

### To All Connecticut Physicians

About four years ago the Connecticut State Medical Society House of Delegates authorized the organization of a political action arm. At that time, the concept of physicians' participation in the political arena was a new one and, in fact, it is still new today.

Unfortunately, some of our colleagues felt that COMPAC and AMPAC (The American Medical Political Action Committee) were organized for the sole purpose of defeating Medicare legislation. No political action committee can be organized as a fire brigade which is called out after a disaster has occurred. Rather, our goal was to develop a strong political voice in this country to protect and extend the private practice of medicine as we know it. Thirty years of effort by organized labor has shown us that political success does not happen overnight. It must be worked at and nurtured.

To point up the importance of these vital endeavors, and to enlist the broadest possible support for them from the profession, COMPAC and AMPAC dues are, for the first time, being included on the 1966 membership dues statements of the Connecticut State Medical Society and its component County Medical Associations. This procedure was approved by the Society's House of Delegates on December 9, 1965, and follows the pattern already set by a majority of the other forty-nine constituent state societies of the American Medical Association.

The purpose of this report is to give you some idea of future political roadblocks which medicine still must face.

### Here Are Labor's Political Goals!

In the April 1965 issue of *AGENDA*, which is published by the Industrial Union Department of the AFL-CIO, several key points in union's plans to meet the health care needs of the people are listed. This partial forecast of labor's political goals *points up heavy participation and control by both government and labor of the practice of medicine*. Here are some examples:

1. Standardize medical and dental fees and eliminate the fee for service system of paying for medical care.
2. Extend health insurance to cover the entire population including office, home and hospital care. (Although a sop is thrown to the private insurance companies, the intent of the article clearly indicates that *this could best be accomplished through a compulsory,*

*publicly-operated government program, i.e., Medicare*).

3. Promote group medical practice in health centers as the prevailing pattern for provision of medical care in town and country.
4. Rationalize the production and distribution of drugs according to scientific principles and reduce the vast extravagance of drug advertising except as necessary to inform the physician.

### Political Action Affects Both State And National Legislation

Those individuals who are knowledgeable about matters political are convinced—and they have convinced us—that it is impossible to carry on any continuous dialogue with political and legislative leaders *without* an effective political action arm.

Here, in Connecticut, we saw numerous cases in point during the last two sessions of the General Assembly. Strong behind-the-scenes political action in support of the State Medical Society's 1965 Legislative Program insured the passage of the Fluoridation Bill, for which COMPAC received a Good Citizenship citation from the Public Health Council, and defeated two potentially dangerous chiropractor bills. In 1963 COMPAC played a key role in the passage of the Animal Research, Good Samaritan and Privileged Communications bills.

The chiropractor proposals would have allowed chiropractors to flood into Connecticut without taking an appropriate state examination and also would have forced smaller communities in many cases to appoint chiropractors as school physicians, medical examiners, health officers etc. Since one of these bills had already passed the State Senate, only a concerted state-wide telephone campaign by PAC members to their political contacts insured defeat of these proposals in the House.

### There Is A Long War Left To Fight!

For those who are discouraged because Medicare is now the law of the land, we point out that although the opening battle may be over, labor's political goals clearly indicate there is a long struggle left . . . on both the national and the state level . . . to defend freedom in medicine.

1/18/66

Respectfully submitted,

THE COMPAC BOARD OF DIRECTORS

FRANCIS GALLO, M.D., *Chairman*



# FROM THE GENERAL MANAGER'S OFFICE

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## CALL

### ANNUAL MEETING OF THE HOUSE OF DELEGATES

The 1966 Annual Meeting of the House of Delegates will be held at the Statler-Hilton Hotel, Hartford, commencing at 10:00 o'clock in the morning of Tuesday, April 26.

Following luncheon, the House will reconvene for the completion of business.

James R. Cullen, President  
Kenneth F. Brandon, Speaker of the House  
Waldo E. Martin, Secretary

### INTRODUCTION OF RESOLUTIONS

Article V, Section 12, Par. 3 of the Bylaws of the Society Provides that:

All resolutions to be considered as regular business at any regular meeting of the House of Delegates must be in the hands of the Speaker not later than seventy-two hours before the opening of that meeting. All resolutions and recommendations published in the official agenda distributed to the members of the House prior to the meeting at which action is to be taken shall be considered as regular business. Resolutions presented later than seventy-two hours before the opening of a meeting will be referred for consideration as regular business by the House only when they are presented by the Council or accepted for consideration by majority vote of the delegates present. Any resolution which does not qualify in accordance with the aforesaid provisions for consideration as regular business may be accepted for action by a majority vote of the delegates present and, if so accepted, shall be referred at once by the Speaker to a reference committee. Any such reference committee shall consider resolutions referred to it and shall report, with recommendations to the House before adjournment of the meeting.

### Delegates To Annual Meeting

The Bylaws of the Society provide that each county association is entitled to one delegate in the House of Delegates for each thirty-five Active or Life Members in the association or fraction thereof based on the membership as of December 31st of the immediately preceding year. According to this, the quota of delegates from each county association who should attend the Annual Meeting of the House of Delegates which will be held in Hartford, April 26, 1966, and the Semi-Annual Meeting in December, 1966, is as follows:

| County     | Membership<br>Dec. 31, 1965 | Official<br>Delegates |
|------------|-----------------------------|-----------------------|
| Fairfield  | 944                         | 27                    |
| Hartford   | 1115                        | 32                    |
| Litchfield | 140                         | 4                     |
| Middlesex  | 118                         | 4                     |
| New Haven  | 992                         | 29                    |
| New London | 198                         | 6                     |
| Tolland    | 26                          | 1                     |
| Windham    | 73                          | 3                     |

### Election Of Councilors And Associate Councilors

Councilors and Associate Councilors, who shall serve for two years, shall be elected this year at the

annual meeting of each of the county associations in Fairfield, New Haven, Litchfield and Tolland counties. In accordance with the Bylaws, each component association having over 750 members may elect one additional Associate Councilor. Therefore the Fairfield and New Haven County Medical Associations should elect a Councilor and two Associate Councilors each for a two year term.

No Councilor or Associate Councilor elected by a component association shall serve more than three successive terms of two years each in his respective office, but after a lapse of one term of two years, such Councilor or Associate Councilor shall be eligible for reelection.

Newly elected Councilors and Associate Councilors shall not assume office until after the Annual Meeting of the House of Delegates.

\* \* \*

At the Semi-Annual Meeting of the House of Delegates on December 4, 1962, Article VII, Section 2 of the Bylaws of the Society was amended by the addition of the following sentence after the term Councilor-at-Large:

"In the event that both the Councilor and the Associate Councilor(s) from a county association cannot be present, the President of the county association may appoint a substitute councilor."

## PLACEMENT WANTED

**DERMATOLOGIST** — Broad background, with extensive training. Seeks group association, position or desirable practice location upon completion of residency in June, 1966. Board eligible.

**GENERAL SURGEON** — Board certified, sub-specialty training in Head and Neck Surgery. Especially interested in Derby-Ansonia or Danbury area.

**INTERNIST**—35 years of age, Board eligible, Connecticut license. Sub-specialty training in Gastroenterology, Endoscopy, Small Intestinal Biopsy. Wishes to associate with an established physician or group.

**INTERNIST**—Board certified, 33 years of age, military obligations completed. Would like to practice in a medium to large community with associate or group, but will consider solo practice as well. Available as of January 1.

**OBS.-GYN.**—Board eligible Obs.-Gyn. with Connecticut license wishes to locate in practice in Connecticut with either a partner or group. Will consider solo practice also. Available immediately.

**PATHOLOGIST** — Board certified in Clinical Pathology and eligible in Anatomic Pathology and Internal Medicine, Connecticut license, with degree in Public Health, wishes to locate in Connecticut in a situation that will allow full use of diversified training.

## PLACEMENT OPPORTUNITIES

**ANESTHESIOLOGIST** — Board certified or Board eligible Anesthesiologist to serve in 65 bed, fully accredited rural hospital which takes care of two communities of about 40,000 total population.

**WANTED**—A young general practitioner trained in Pediatrics to share in fully established practice. Two fully accredited hospitals totaling over 700 beds serve this area. Address inquiries to: P.O. Box 469, Woodbury, Connecticut.

**INDUSTRIAL PHYSICIANS** — Two physicians qualified in Internal Medicine with some knowledge of Surgery for two large, respected national firms to serve on corporate staff. The firms are located in Hartford, Connecticut area. Regular hours, 38 hour week, salary range \$16-\$18,000 plus full benefit program.

G.P.'s needed for the Meriden-Wallingford area for private practice in this rapidly growing, industrial area of Connecticut. For further information, contact M. J. Esposito, M.D., 335 Cook Avenue, Meriden, Connecticut.

**MEDICAL GROUP** has position for a general practitioner and internist. Call or write Chapel Medical Group, 1308 Chapel Street, New Haven, Connecticut 06511.

**PATHOLOGIST** — Full or half-time to direct clinical laboratory in a 2300-bed mental hospital. Ample opportunity for teaching and research available. Well equipped and staffed laboratory. Emphasis on neuropathology. Board certified or eligible pathologist preferred. Salary range: \$14,740-\$19,100. Fringe benefits: 3 weeks' paid vacation, 3 weeks' sick leave paid, 11 paid holidays, free Blue Cross, CMS and Major Medical insurance. Contact John F. Lowney, Jr., M.D., Superintendent, Connecticut Valley Hospital, Middletown, Connecticut.

**CLINICAL DIRECTOR**—for Medical-Surgical Service in a decentralized 2300-bed mental hospital. Active teaching program in psychiatry. Affiliated with Yale University. Fully staffed medical service. Board certified or eligible internist preferred. Salary range: \$15,460-\$20,000. Fringe benefits: 3 weeks' paid vacation, 3 weeks' paid sick leave, 11 paid holidays, free Blue Cross, CMS and Major Medical Insurance. Contact John F. Lowney, Jr., M.D., Superintendent, Connecticut Valley Hospital, Middletown, Connecticut.

**INTERNIST** — Board eligible or certified Internist with sub-specialty training in Gastroenterology wanted to join a multi-specialty group in New Britain. Connecticut license eligibility or license required.

**WANTED** — House Physician—diversified duties in accredited, voluntary hospital. Connecticut license required—no weekends. \$15,000 yearly. Please reply to: P. O. Box 638, Bridgeport Connecticut 06601.

**ANYONE INTERESTED IN THE ABOVE IS ASKED TO CONTACT THE GENERAL MANAGER'S OFFICE, 160 ST. RONAN STREET, NEW HAVEN, CONNECTICUT 06511.**

## 1966 MEETINGS

**March 24** — 182nd Annual Meeting of the New Haven County Medical Association to be held at the Waverly Inn, Cheshire, Connecticut. Business Meeting tentatively set for 3:30 P.M.

**April 26-28** — 174th Annual Meeting of The Connecticut State Medical Society to be held at the Statler-Hilton Hotel, Hartford, Connecticut.

**September 28** — 41st Clinical Congress to be held at the Yale-New Haven Medical Center.



## ARTISTS, ATTENTION

The Connecticut Physicians Art Association is planning the 1966 Art exhibit in conjunction with the Annual Meeting of the Connecticut State Medical Society. This will be held at the Statler Hilton, Hartford, Connecticut, on April 26, 27, 28, 1966.

All previous exhibitors are invited to show their works at this meeting and new exhibitors among physicians and their families are cordially invited to join the group of art hobbyists. Works eligible will include oil, water color, tempora, black and white, etchings, photography, pastels, sculpture and ceramics. Eligible exhibitors are members of the Connecticut State Medical Society, their wives, and children. Art works will be judged in four categories: 1. children through 16 years (over 16 will be judged with adults); 2. Beginners to three years; 3. Over three years; 4. Professional.

A hanging fee of one dollar (\$1.00) will be charged for each entry and fifty cents (\$.50) for children under 16 with three pictures allowed per artist. Pictures should be framed and wired for hanging. The exhibition will be judged by professional artists.

Entry blanks will be mailed to former exhibitors and may be obtained by writing to the below address. A special effort will be made to recognize merit in each group so it is important to fill in the entry blank completely stating the number of years that you have been enjoying this hobby. Professional artists are welcome and will be judged in the professional class.

Art works must be submitted to a representative of the Art Association in the lobby of the Statler Hilton on Sunday, April 24th (hours will be announced later). Please forward entry blanks and checks to the address below prior to April 15th (make checks payable to the "Connecticut Physicians Art Association").

After several years lapse, we are all quite hopeful of having a most successful show. Please watch subsequent issues of CONNECTICUT MEDICINE for further details and information regarding this exhibit.

Stewart J. Petrie, M.D., President, Connecticut Physicians Art Association.

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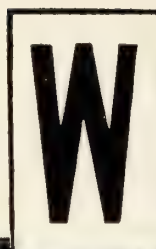
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## ACCENT ON THE COUNTIES ANNUAL REPORT OF THE WOMAN'S AUXILIARY TO THE NEW HAVEN COUNTY MEDICAL ASSOCIATION—1965

We know that you will be pleased with New Haven County's accomplishments during our 20th Anniversary Year. As you know, we took the occasion of this milestone year to re-examine our many interests and designate those which we felt should receive maximum attention. These were considered "Priority Projects."

Among them were the community service projects. Secondary school assembly programs were arranged by the committee on health careers. These programs were enthusiastically received and did much to focus the attention of students on the challenge and reward in health service careers.

Another community service project was the arranging of teas by the mental health chairman every month at the Veterans Hospital in West Haven. Members of the New Haven Auxiliary served tea to over 150 patients who looked forward to these pleasant afternoons.

AMA-ERF was another interest to which the Auxiliary devoted maximum attention. We raised our AMA-ERF gift last year to \$537.00, averaging \$3.00 per member. This was a considerable increase over our previous annual contributions—and nearly double the amount of the prior year's gift.

Perhaps the most exciting and rewarding aspect of the year was the success of our scholarship benefit. A dinner-dance was held on March 6th, at the Holiday Inn. Proceeds for scholarship were further enhanced by a special anniversary ad booklet in which we included a "Twenty Years Young" history of our Auxiliary. Thanks to the dedicated efforts of a relatively few doctors' wives, the profit from our scholarship benefit was \$1452.00—a new record for New Haven County.

The scholarship trustees awarded \$1250.00 in scholarships to 11 high school seniors, chosen on the basis of personal need, interest, scholarship and character. The girls represent a variety of schools and have selected diversified health careers. These winners are from the following towns within New Haven County: 1 each from West Haven, East Haven, Orange, Madison, Hamden, Ansonia, Southbury, Derby, Milford and 2 from Waterbury, and have selected careers of study as follows: 1 dietician, 1 occupational therapy, 1 physiotherapy, 1 teaching of the mentally retarded, and 7 will pursue careers in nursing. Three of the award recipients will begin studies at Grace-New Haven School of Nursing, and 1 at each of the following: Simmons College, Greenwich Hospital, University of Connecticut, Boston University, Northeastern University, Southern Connecticut, St. Vincent's Hospital and Norwalk Hospital.

We also chose last year to launch an all-out drive for increased membership. A Newsletter was mailed to all wives of County Medical Association members describing our aims and activities and emphasizing the scope of auxiliary services. Our efforts resulted in the addition of 53 new members, bringing our total membership to 179. This means that 30 per cent of our current membership was new last year. Our programs were varied in hopes of gaining the widest possible appeal. Mrs. John Lodge spoke at our fall meeting, and Dr. Christie McCloud, Chief of Pathology at the Middlesex Hospital, spoke on her trip to Russia at our annual meeting.

We feel that New Haven County put forth great effort last year to demonstrate the effectiveness of the work of the Auxiliary. It was an exciting and

rewarding 20th Anniversary Year. We hope to continue to play a vital role as a liaison between the medical profession and the community. We welcome *all* doctors' wives—those who lend active participation *and* those who are able to give us only moral support at this time. Right now the burden of work and struggle for accomplishment has fallen on the shoulders of a relatively few. *We earnestly need your support.* This is your organization—help make this next year significant and successful!

Sincerely yours,

MRS. ARNOLD M. BASKIN, *President*

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## BOOKS RECEIVED

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*Books received for review are acknowledged in this department and such acknowledgement must be regarded as a sufficient return for the courtesy of the sender. Selection will be made for review in the interests of our readers and as space permits.*

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*Respiratory Care.* H. H. Bendixen, et al. From the Respiratory Unit and the Anesthesia Laboratory of the Harvard Medical School at the Massachusetts General Hospital, Boston, Mass., 1965. 252 pp. Illustrated. \$15.00.

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*Controversy In Internal Medicine.* Edited by Franz J. Ingelfinger, M.D., Arnold S. Relman, M.D. and Maxwell Finland, M.D. The W. B. Saunders Co., Philadelphia and London, 1966. 679 pp. \$14.50.

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*Ferment In Medicine.* A Study of the Essence of Medical Practice and of Its New Dilemmas. Author: Richard M. Magraw, M.D. With a chapter on Automation in Medicine written in collaboration with Daniel B. Magraw, M.B.A. W. B. Saunders Co., Philadelphia and London, 1966. 272 pp. \$6.50.

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*Fundamentals Of Clinical Hematology.* Second Edition. Authors: Byrd S. Leavell, M.D. and Oscar A. Thorup, Jr., M.D. The W. B. Saunders Co., Philadelphia and London, 1966. 597 pp. Illustrated. \$12.50.

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Health insurance policies cover about 78 percent of the U. S. population. Benefits paid on these policies reached \$8.6 billion in 1964. Government programs in 1964 paid about \$1.2 billion in health aid to the vendors of health services.

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Forty percent of the nation's physicians are responsible for writing 80 percent of the prescriptions.

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## In Memoriam

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**Aey, Arthur E.**—Norwich; University of Pennsylvania Medical School, 1943. Dr. Aey was a general practitioner in the Norwich area for over ten years. He was a member of the New London County Medical Association, the Connecticut State Medical Society, and the American Medical Association. Dr. Aey died December 17, at the age of 47.

**Appell, Harold S.**—New Haven; Tufts Medical School, 1927. Dr. Appell practiced medicine for 38 years, specializing in dermatology. He was on the staff of the Yale-New Haven Hospital. Dr. Appell served during World War II, as a naval surgeon with the rank of lieutenant commander. Until recently, Dr. Appell taught for more than ten years at the New York Skin and Cancer Unit of Columbia University. He was a member of the New Haven Medical Association, the New Haven County Medical Association, the Connecticut State Medical Society, the American Medical Association, and the American Board of Dermatology and Sphilology. Dr. Appell died January 11, at the age of 63.

**Capecelatro, Alfonso**—New Haven; Tufts Medical School, 1919. Dr. Capecelatro was a member and past president of the St. Raphael Hospital medical staff. He served with the Army Medical Corps during World War I. He was a member of the New Haven Medical Association, the New Haven County Medical Association, the Connecticut State Medical Society, and the American Medical Association. He was a fellow of the American College of Surgeons and a diplomat of the International College of Surgeons. Dr. Capecelatro died January 10, at the age of 78.

**Sloman, Howard S.**—Baltimore, Maryland; New York University School of Medicine, 1948. Dr. Sloman served with the U. S. Army Medical Corps as a captain. He was an associate of the American College of Physicians and while in Connecticut was an attending physician at the Norwalk Hospital. Dr. Sloman was a member of the Fairfield County Medical Association, the Connecticut State Medical Society, and the American Medical Association. Dr. Sloman died November 11, at the age of 40.



## Special Notices

### MEDICAL AND SURGICAL SHOCK SYMPOSIUM

February 18, 1965

Memorial Building — 11:30 A.M. — 2:00 P.M.

The Medical Service, in conjunction with the Medical Education Committee of The Charlotte Hungerford Hospital, Torrington, will present a symposium on "Medical and Surgical Shock."

Speakers will be Roger Hickler, M.D., Professor of Medicine, Harvard Medical School; Nicholas Green, M.D., Professor of Anesthesiology, Yale Medical School; and Allen Goodyer, M.D., Professor of Medicine, Yale Medical School.

The symposium, as stated is scheduled to begin at 11:30 a.m. and continue to 2:00 p.m. Luncheon will be served.

### THREE DAY POSTGRADUATE COURSE NO. 12

"Pathogenetic Mechanisms in Cardiovascular Disorders"

Columbia Presbyterian Medical Center

New York, New York

March 14-16, 1966

Subject course co-directed by Doctors Alfred P. Fishman and Glenn A. Langer, is being sponsored by the Council on Clinical Cardiology and the Columbia Presbyterian Medical Center in cooperation with the New York Heart Association.

Registration Fees of \$50.00 for Fellows and Members of the Council on Clinical Cardiology, and \$85.00 for Non-Members are on a first-come, first-served basis. Checks should be made payable to the American Heart Association and sent to Mrs. Lorraine Kreiner, Council of Clinical Cardiology, American Heart Association, 44 East 23rd St., New York, N. Y. 10010, as early as possible.

All sessions will be held in the Alumni Auditorium, College of Physicians, 630 West 168th St., New York, N. Y.

In addition to Columbia-Presbyterian Medical Center Faculty Speakers, the program includes talks by visiting physicians Lewis Dexter, M.D., Asst. Prof. Department of Medicine, Peter Bent Brigham Hospital—Boston; Julius H. Jacobson, II, M.D., Director of Vascular-Surgical Service, Mt. Sinai Hospital—New York; Daniel S. Lumas, M.D., Assoc. Prof of Medicine, Cornell University; Norman Rosenberg, M.D., Clinical Professor, Department of Surgery, Rutgers University, New Brunswick, N.J.; F. Mason Somes, M.D., Director, Cardiac Laboratory, Cleveland Clinic-Cleveland; and David M. Spain, M.D., Director, Department of Pathology, Brookdale Hospital Center, Brooklyn, New York.

Following registration at 9:00 A.M., Monday, March 14, Dr. H. Houston Merritt, Dean, College of Physicians and Surgeons, Department of Neurology, Columbia Presbyterian Medical Center, will make the opening remarks. The morning session will cover various aspects of "The Heart and Heart Failure," and the afternoon session will discuss "Cor Pulmonale."

On Tuesday, March 15, the morning session will be devoted to related subjects covering "Arteriosclerosis and its Complications," and the afternoon session to "Practical Electrophysiology."

Closing the three-day conference, Wednesday, March 16, subjects discussed in the morning and afternoon sessions will relate to "Special Clinical States" and "Recent Advances in Cardiovascular Diagnosis and Treatment."

## Letter To The Editor

### To the Editor:

All physicians in Connecticut and their families are invited to participate in the program of education and public information conducted by the Connecticut Society for Medical Research, which has been described in correspondence to *CONNECTICUT MEDICINE*, Vol. 29, No. 12, December, 1965.

Support as individuals is possible in the categories listed below. If you are not a member, or if others in your family wish to obtain membership in CSMR, please clip and mail the application below.

GEORGE MURDOCK, *President*

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*Letters to the Editor are welcome and will be published for informative and educational purposes as space permits. As with other material which is submitted for publication, all letters will be subject to the usual editing. Address all correspondence to: THE EDITOR, CONNECTICUT MEDICINE, 160 St. Ronan Street, New Haven, Connecticut, 06511.*

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## Doctor's Office

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Willet R. Bowen, M.D., announces the opening of an office for the practice of pediatrics on Rt. #7, Brookfield.

J. Clement Griffin, M.D., announces the opening of an office for the practice of ophthalmology at 206 Washington Street, Norwich.

Francis J. Kenney, M.D., announces the removal of his office for the practice of thoracic and cardiovascular surgery to 1211 West Main Street, Waterbury.

Patrick H. McDonagh, M.D., announces the opening of an office for the practice of psychiatry at 2044 Bridgeport Avenue, Milford.

Michael F. Nezhad, M.D., announces the opening of an office for the practice of internal medicine and gastroenterology at 1389 West Main Street, Waterbury.

Bernard Passman, M.D., announces the opening of an office for the practice of obstetrics and gynecology at 49 Connecticut Boulevard, East Hartford.

John F. Summa, M.D., announces the removal of his office for the practice of cardiovascular disease to 159 Grove Street, Waterbury.

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### 174th Annual Meeting

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### A Request For Change of Address

must reach us at least three weeks before the date of issue with which it is to take effect. Please be sure to send us the old address, together with the new address.

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## NEW BOOKS IN REVIEW

**HANDBOOK OF PHYSICAL MEDICINE AND REHABILITATION.** Edited by Frank H. Krusen, M.D. Associate Editors: Frederick J. Kottke, M.D., Paul M. Ellwood, Jr., M.D. The W. B. Saunders Company, Philadelphia and London, 1965. 725 pp. Illustrated. \$16.50.

Reviewed by: SIDNEY LIGHT

Too often we read at the end of a book review, "This book belongs in every library." For the book under consideration such a cliché would be incomplete. This book should be required reading for anyone in or entering the field of physical medicine and rehabilitation. Any physician who treats patients with chronic illness will be more effective if he masters the information in this helpful book. Not all the contributors are well known but almost every participant knows well the subject on which he has written. Among the outstanding chapters are those on neurologic diseases, bed positioning and homemaking activities. The chapter which towers above all others is that on vocational assessment and management. The author gives the limitations and goals of rehabilitation in basic English and in terms of common sense.

This is the first entirely new book in more than five years in this rapidly expanding field. Not too long ago it would have been possible to cover the pertinent knowledge in one book. This is no longer possible, as witness the multitude of books bearing as their titles the chapter headings of this book. At least one such book is longer than this handbook. There is virtually no "padding" in this book; in fact, if the book can be faulted, it is for its thriftiness. In almost every chapter, this reviewer felt that the story was incomplete; most chapters are introductions—of high quality, but offering only part of the story.

Williams' exercises are mentioned in one chapter without any reference to the original or later description. (Williams did not write a book or article but a chapter of a book with limited circulation.) Many chapters later there is a picture of Williams' exercises not mentioned in the chapter text. This is one of the very few examples of inadequate editing. Most of the book demonstrates editing of the highest order; there is a minimum of repetition and a good amount of cross pagination reference. Most of the illustrations are well chosen and clear. It is unfortunate that the publisher used offset instead of letterpress; a few of the photographs are not well reproduced.

A book of this quality must one day appear in second edition. The criticisms offered are for that occasion. We believe that the index is not sufficiently inclusive. The word *orthotic* is not present in any of its many variants, nor do we find such words as cold, ice or traction. Some of the chapter titles are not satisfactory. The chapter called evaluation of gait is largely about orthotics and prosthetics.

Since there are a dozen times as many physical therapists as physiatrists, there is the temptation to key the writing of texts in this field to the potential market. The writers of this

book did not "talk down" to the reader. On the contrary, many readers will be forced to consult a dictionary or the literature in search of definitions and explanations.

This book is a welcome addition to the literature of physical medicine. The problem which remains is to convince physicians to read it.

**RHEUMATIC FEVER: DIAGNOSIS, MANAGEMENT AND PREVENTION.** Vol. II in the series of *Major Problems in Clinical Pediatrics*. Alexander J. Schaffer, consulting Editor, Milton Markowitz, Ann Gayler Kuttner, with a special chapter on community Health Services by Leon Gordis. W. B. Saunders Company, Philadelphia and London, 1965, 242 pp. Illustrated. \$7.50.

Reviewed by: LOUIS H. NAHUM

Acute rheumatic fever must be viewed as a potentially preventable complication of streptococcus infections provided patients seek medical attention and receive adequate diagnosis and treatment. It follows that with the knowledge currently available physicians can reduce the incidence of severe rheumatic heart disease and by preventing initial attacks, eventually make rheumatic fever a truly rare disease.

In this monograph the biology of group A streptococci is briefly reviewed and the serologic and epidemiologic data that link this organism with rheumatic fever are summarized. The changing pattern, the clinical manifestation, diagnosis and treatment as well as the regimes effective for the prevention of recurrences and treatment of initial attacks are authoritatively discussed.

The authors examine the question of pathology, etiology and pathogenesis in detail pointing out what is known and what remains to be learned in these areas. The pathology of the nodule and its close relation to intravascular clotting is not thoroughly explored although it may turn out that a fibrinolytic agent could well contribute to minimizing the ravages of the disease, especially in the heart, once a drug with fibrinolytic properties became available. In fact it is our inability to prevent the consequences of intravascular thrombi that makes our present therapy so inadequate. But perhaps it is a little too early in our knowledge to explore this area.

There are knotty problems of diagnosis, differential diagnosis, and treatment which are clarified by the authors who have been confronted with these situations many times a week for many years.

All the worthwhile information on this subject is assembled here and combined with the authors rich funds of experience in a form which renders this monography immediately useful to the physician and pediatrician. By referring to this book any physician can treat a case of rheumatic fever in any stage authoritatively. The authors have produced a fine guide for the medical profession.



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## Nutrition Lectures Planned For Three Connecticut Colleges

The Connecticut State Medical Society, in co-operation with the American Medical Association, will co-sponsor a clinical nutrition lecture in three colleges during the month of March.

Dr. Nevin S. Scrimshaw, Professor and Head of the Department of Nutrition and Food Science, Massachusetts Institute of Technology, will deliver the lectures and the topic will be "Food and Nutrition in the Future."

The lectures will be presented at Willimantic State College, Willimantic, on Thursday, March 3, at 12:00 noon; Quinnipiac College, Hamden, Tuesday, March 15, at 12:30 P.M.; and at Southern Connecticut State College, New Haven, in late March on a date to be announced.

The AMA's Council on Foods and Nutrition initiated the clinical nutrition program during the last academic year and it is being carried out in the regions of the United States with several prominent lecturers participating.

The lectures are planned to stimulate undergraduate students to consider careers in the health sciences and to inform students of new developments in nutrition.

Thirty-six lectures have been scheduled in the regional four-state area which includes Connecticut, New York, Ohio, and Pennsylvania.

## Hospital Staffs To Get Handbook On Utilization Review

*Utilization Review—A Handbook for the Medical Staff* was distributed by the American Medical Association to the chiefs of staff of all nonfederal, short-term, and other special hospitals.

Developed by the AMA's Department of Hospitals and Medical Facilities at the direction of the Committee on Medical Facilities of the Council on Medical Service, the Handbook is intended to assist in carrying out the recommendation that medical staffs of hospitals be urged and assisted to form utilization committees, as adopted by the AMA House of Delegates at the December 1964 Clinical Convention.

Copies of the Handbook will also be furnished to state and local medical societies.

The Handbook presents a collection of various references on utilization review. It includes the text of the July 1965 revision of the *Guide to the Establishment and Functioning of a Medical Staff Utilization Committee* prepared by the Hospital Utilization Project of Western Pennsylvania.

## Computer Becomes A Blood Banker

For several months, a computer has been keeping the records of a large blood bank in Oakland, California—and it's doing a good job, reports Journal of the American Medical Association.

The system was worked out by the Blood Bank of the Alameda-Contra Costa Medical Association and Lockheed Missiles and Space Company.

So far, the computer has been able to reduce the bank's inventory of blood 15 to 20 per cent while continuing to serve 28 hospitals with a total of 4,600 beds.

Outdated blood, a costly loss in any blood bank, has been cut from more than 13 per cent of inventory to less than 6 per cent.

As another sign of tightening inventory control, the average age of transfused blood has been reduced from 10.7 to 9.5 days since February 1965.

The system works this way:

Each of 28 hospitals in a two-county area phones its daily blood consumption total to the blood bank, where the information is punch-coded onto paper tape, and transmitted to the Lockheed computer center 50 miles away.

Back from the computer comes a summary of each hospital's report. The computer not only keeps a running total on the blood inventory, but also warns when blood stocks are aging. Losses are cut by transferring this blood to hospitals where it can be used immediately.

Once a week, the computer lists each hospital's average usage by blood type. These reports help reduce inventories to a minimum.

A monthly summary outlines the source and use of every pint of blood. Still another report keeps an eye on human error as data are fed to the computer.

It requires 30 people to handle the 34,000 pints of blood dispersed each year by the blood bank. None of these have been replaced by the computer, the report said, but they have been relieved of the tedium of routine record-keeping.

The computer system is costly, but its efficiencies should repay these costs if widely applied to blood banking, the Journal report said. The system's design appears to be applicable to all blood banks, regardless of size or location.

Authors of the Journal report are David Singman, M.D., Calisto A. Catassi, C.P.A., and Charles R. Smiley, of the Blood Bank; Willard H. Wattenburg, Ph.D., of the Department of Electrical Engineering, University of California, Berkeley, and Eric L. Peterson, M.B.A., Lockheed Missiles and Space Compny, Sunnyvale, Calif. (Mr. Smiley is now with Hyland Laboratories, Los Angeles.)



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|-------|------|-------|
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## **AMA Journals Have Foreign Circulation Of Nearly 40,000; Play Major Role In Disseminating U. S. Medical Knowledge**

The most famous of American medical journals, the weekly *Journal of the American Medical Association*, is distributed to more than eight thousand paid foreign subscribers in 123 countries. The 10 monthly AMA specialty journals (dermatology, surgery, internal medicine, diseases of children, environmental health, general psychiatry, neurology, ophthalmology, otolaryngology, and pathology) go to more than 16 thousand paid foreign subscribers. Nearly two thousand copies of the *AMA News*, a newspaper of non-scientific medical news for physicians, goes to selected foreign subscribers, and *Today's Health*, the AMA medical publication for laymen, has a paid foreign circulation of nearly 10 thousand.

Thus, the publications of the AMA alone have a paid foreign circulation of nearly 40 thousand. (Total domestic and foreign *Journal* circulation is 212,504 per week; total specialty journal circulation is 222,307 per month.)

As the journal of American medicine, the *Journal of the AMA* (known to American doctors as *JAMA*) appeals to as broad a range of interests in foreign lands as it does in the United States.

Foreign practitioners value *JAMA* as a part of their continuing medical education. In its attention to drugs and drug therapy, for example, *JAMA* is invaluable to the foreign doctor who has access to American-made drugs.

In 1965, *JAMA* also published such papers as these:

—A listing and medical evaluation of all fertility control devices widely available in the United States. Published under the sponsorship of the AMA Committee on Human Reproduction, the paper represents the considered opinion of a number of medical authorities.

—An article on homosexuality and the physician's role in prevention and treatment.

—A multi-part series on current concepts in cancer detection and treatment.

—A monthly feature on bone fractures.

—Many articles on medical education, including considerations of medical education in developing nations.

Foreign subscribers to specialty journals found articles like these in 1965:

—A new treatment to combat infection in severe burns, based on the use of silver nitrate on burned areas. Developed at Washington University and hospitals in St. Louis, the treatment was reported in the journal *Archives of Surgery*.

—A symposium on German measles (rubella), the usually mild viral disease that can cause congenital malformations in the unborn child of an infected mother-to-be. It was published as the entire October edition of the *American Journal of Diseases of Children*.

To a British physician on Harley Street, *JAMA* and the specialty journals may be necessary check points in a week of "keeping up with the journals." British physicians, like American, probably read 10 to 20 medical publications regularly. To a physician practicing in Southeast Asia, though, a single copy of *JAMA* at the local hospital may be a most valued contact with current medical thought. Some underdeveloped nations receive only one or two copies of *JAMA* through paid subscriptions, and these often go to a hospital; but the AMA Department of International Health estimates that nearly every English-speaking doctor and medical technician having access to the "hospital copy" makes an attempt to read every issue. The estimate is made on the basis of conversations with foreign doctors visiting the U. S., and with U. S. physicians returning from service in underdeveloped nations.

Nearly every major medical school and medical library in the world also gets at least one copy of *JAMA* for teaching and reference. Information volunteered to the AMA Department of International Health by foreign physicians indicates that a single library copy of *JAMA* may go through the hands of 40 or more readers.

Through *JAMA*, the AMA specialty journals, and other professional publications physicians in Iron Curtain countries keep in close touch with American medical trends.

A number of Communist nations, including isolationist Albania, Bulgaria, the Soviet Union, and Mainland China, receive from one to a dozen copies of *JAMA* weekly. Most of the copies go to medical schools, where, according to the AMA Circulation and Records Department, they often are duplicated for wider distribution. Although the published material in *JAMA* is protected by copyright, the Soviet Union and some other Communist states do not recognize copyright regulations.

As an indication of the extent to which the Soviet Union duplicates *JAMA*, only six paid-subscription copies are sent to the USSR but nearly every Russian physician who visits the United States confides that he is a regular *JAMA* reader.

Hundreds of American medical missionaries in foreign lands receive *JAMA* and other AMA publications free of charge. The AMA furnishes the publications as a means of permitting these dedicated doctors to stay abreast of medical developments and remain in contact with main currents



of American medicine, despite their isolation from medical centers. JAMA circulation to some countries—the Congo and New Guinea, for example—is all or nearly all of this non-paid type.

Some examples of JAMA paid-subscription circulation throughout the world:

—1,135 copies go to Canada. More than 200 of these are to Montreal, and hundreds more to Toronto, Ottawa, and other major centers of Canadian population. In the vast northern areas of Canada a number of doctors are served by a hospital “single copy”: one such example is the single copy of JAMA sent to Whitehorse General Hospital, Whitehorse, Yukon Territory. Paid-subscription circulation of all AMA publications in Canada is 12,045. (Canada has about 22,600 physicians, according to World Health Organization statistics.)

—The four JAMA copies going to Afghanistan are received by two U. S. Peace Corps physicians, a UNICEF Public Health Institute in the Ministry of Health, and an American medical team operating on funds from a private U. S. organization.

—A single copy to Ocean Island in the Central Pacific, received by the British Phosphate Commission.

—Four Bulgarian medical institutions get five paid-subscription copies.

—Circulation in Viet-Nam (six paid-subscription copies and many more free copies) is divided among hospitals, individual Vietnamese doctors, medical missions, American physicians serving in Project Viet-Nam, and the American Embassy in Saigon.

—The 10 foreign nations with highest JAMA circulation are Canada, 1,135; Italy, 777; Japan, 671; England, 346; India, 338; Holland, 318; Mexico, 298; France, 275; West Germany, 260; Sweden, 250.

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### **Holmes And Hippocrates—Proven Wrong?**

We have in a sense been caught by our own ingenuity. The day is past when we could say, as Oliver Wendell Holmes did, “Throw out opium . . . throw out a few specifics which our art did not discover . . . throw out wine . . . and I firmly believe that if the whole materia medica, as now used, could be sunk to the bottom of the sea it would be all better for mankind—and all the worse for the fishes.” We cannot afford to do without good, new drugs. We can no longer say, as did Hippocrates, “. . . as to diseases make a habit of two things— to help, or at least not to do harm.”—Louis Lasagna, M.D., in *Perspectives in Biology and Medicine*, 7:4, (Summer) 1964.

### **Postgraduate Medical Education Expanding**

Most physicians continue to study medicine long after entering practice—and the number of postgraduate medical courses available to them has increased nearly 50 percent in the past five years.

This year, 1,641 courses are being offered in 40 states and the District of Columbia, reports the current Journal of the American Medical Association. The issue contains the 65th annual report on medical education by the AMA's Council on Education.

The number of physicians registered in these courses may be over 150,000.

Attending courses, however, is only one of the ways a doctor continues his education, the Journal points out. Most physicians rank their continued reading of medical literature as one of their most important sources of new knowledge.

They also continue their education through professional contacts with other physicians, and through hospital staff meetings and national, state and local medical society meetings.

Formal postgraduate courses, however, are becoming increasingly important. Medical schools continue to be the major sponsors, but courses also are offered or co-sponsored by medical societies, voluntary health agencies, hospitals, and governmental health agencies.

The most popular subject when doctors return to class? Psychiatry, by a wide margin. Courses in general medicine come next. Special subject areas such as pathology, surgery, ophthalmology, obstetrics-gynecology, and cardiovascular disease also are popular.

Figures are not now available on the total number of physicians attending continuing education courses. Partial figures indicate that there has been a marked increase since last year.

During the 1964-65 academic year, there were 88,845 registrations at courses sponsored by medical schools. Medical schools sponsor about half the courses. If attendance at other courses was similar, the total registration last year must have exceeded 150,000, the Journal said.

---

### **Drug Efficacy—Who's To Say?**

The (new drug) law should be modified by the deletion of F.D.A. responsibility for “efficacy.” The final approbation or disapproval of a drug should be in the hands of the medical profession and not the F.D.A. In addition, there are many officials of the F.D.A. who should reassess their relationship to the pharmaceutical industry in the light of the sound philosophy that a successful democracy is

more than a form of government; it is a behavior pattern which stems from the "Golden Rule."—John C. Krantz, Jr., Ph.D., in *Military Medicine*, 130:1, (January) 1965.

### Skin Preserved By Deep Freezing

The successful preservation and transplantation of human skin which had been in super-cold storage for up to 608 days is reported in the current Journal of the American Medical Association.

"Skin banks" aren't new, but there has been difficulty in preserving skin for long periods. Human skin quickly deteriorates when merely refrigerated. Hard freezing often destroys the skin's ability to survive when transplanted.

The authors, Ronald B. Berggren, M.D., and Herndon B. Lehr, M.D., of the University of Pennsylvania School of Medicine, Philadelphia, and South Jersey Medical Research Foundation, Camden, describe how they soaked split-thickness skin in protective solutions of glycerol or the experimental drug, DMSO, and then gradually cooled it to temperatures as low as 385 degrees Fahrenheit. A liquid nitrogen freezer was used.

Using skin thus stored, 12 of 26 transplants of the patients' own skin were permanently successful. Six of 12 homografts, or transplants from donors, survived for at least 10 days. There was a high percentage of success when the body areas on which the skin was grafted were in good condition.

When applied side by side on a man's cheek, there was no apparent difference in fresh skin grafts and tissue which had been stored five months, the authors said. The stored skin had been taken for an earlier operation, but had not been used.

An advantage of long-term storage, the authors point out, is that enough skin can be taken from the donor in one operation to supply re-graftings when necessary. This eliminates repeated skin-removal operations.

There still are questions about ultra-cold skin freezing. The storage time is not always predictable. Sometimes skin remains usable for several months; sometimes it deteriorates quickly.

It hasn't been determined yet how cold the freezing must be to keep skin usable. Storage would be simplified, the authors said, if dry ice (minus 174 degrees F.) could be used instead of liquid nitrogen (minus 356 to minus 385 degree F.).

The protective solutions, such as glycerol or DMSO, prevent tissue damage during freezing and thawing. The exact cause of this damage isn't known, but it may be due to ice forming between cells, or the drawing-off of water from cells during freezing. The protective action of glycerol or DMSO may be due to their ability to bind water so that it never forms into ice crystals, the authors said.

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**Contraindications:** Benactyzine hydrochloride is contraindicated in glaucoma. Previous allergic or idiosyncratic reactions to meprobamate contraindicate subsequent use.

**Precautions:** *Meprobamate*—Careful supervision of dose and amounts prescribed is advised. Consider possibility of dependence, particularly in patients with history of drug or alcohol addiction; withdraw gradually after use for weeks or months at excessive dosage. Abrupt withdrawal may precipitate recurrence of pre-existing symptoms, or withdrawal reactions including, rarely, epileptiform seizures. Should meprobamate cause drowsiness or visual disturbances, the dose should be reduced and operation of motor vehicles or machinery or other activity requiring alertness should be avoided if these symptoms are present. Effects of excessive alcohol may possibly be increased by meprobamate. Grand mal seizures may be precipitated in persons suffering from both grand and petit mal. Prescribe cautiously and in small quantities to patients with suicidal tendencies.

**Side effects:** Side effects associated with recommended doses of 'Deprol' have been infrequent and usually easily controlled. These have included drowsiness and occasional dizziness, headache, infrequent skin rash, dryness of mouth, gastrointestinal symptoms, paresthesias, rare instances of syncope, and one case each of severe nervousness, loss of power of concentration, and withdrawal reaction (status epilepticus) after sudden discontinuation of excessive dosage.

*Benactyzine hydrochloride*—Benactyzine hydrochloride, particularly in high dosage, may produce dizziness, thought-blocking, a sense of depersonalization, aggravation of anxiety or disturbance of sleep patterns, and a subjective feeling of muscle relaxation, as well as anticholinergic effects such as blurred vision, dryness of mouth, or failure of visual accommodation. Other reported side effects have included gastric distress, allergic response, ataxia, and euphoria.

*Meprobamate*—Drowsiness may occur and, rarely, ataxia, usually controlled by decreasing the dose. Allergic or idiosyncratic reactions are rare, generally developing after one to four doses. Mild reactions are characterized by an urticarial or erythematous, maculopapular rash. Acute nonthrombocytopenic purpura with peripheral edema and fever, transient leukopenia, and a single case of fatal bullous dermatitis after administration of meprobamate and prednisolone have been reported. More severe and very rare cases of hypersensitivity may produce fever, chills, fainting spells, angioneurotic edema, bronchial spasms, hypotensive crises (1 fatal case), anuria, anaphylaxis, stomatitis and proctitis. Treatment should be symptomatic in such cases, and the drug should not be reinstituted. Isolated cases of agranulocytosis, thrombocytopenic purpura, and a single fatal instance of aplastic anemia have been reported, but only when other drugs known to elicit these conditions were given concomitantly. Fast EEG activity has been reported, usually after excessive meprobamate dosage. Suicidal attempts may produce lethargy, stupor, ataxia, coma, shock, vasomotor and respiratory collapse.

**Dosage:** Usual starting dose, one tablet three or four times daily. May be increased gradually to six tablets daily and gradually reduced to maintenance levels upon establishment of relief. Doses above six tablets daily are not recommended even though higher doses have been used by some clinicians to control depression and in chronic psychotic patients.

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Connecticut State  
Medical Journal

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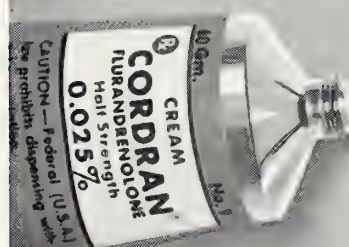
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Other barbiturates, heptobarbital and barbitol have also been shown to stimulate coumarin-metabolizing enzymes in both animals and man.<sup>1</sup> It may be reasonably assumed that most barbiturates will probably have a similar stimulatory effect on liver enzyme induction. An acute study in man showed a decrease in maximum anti-coagulation response of about 60 per cent on pretreatment with heptobarbital for three days before a single dose of 500 mg. of dicumarol was given by mouth. Similar results were obtained using single doses of other coumarin derivatives, such as dicoumacetate and acinocoumarin, after pretreatment with heptobarbital.<sup>1</sup>

Apparently it is not just the barbiturates which can interfere with coumarin action but some other tranquilizers as well. Haloperidol has also been reported to reduce the prothrombin response to phenindione.<sup>4</sup> As the search goes on for drug interference doubtless others will be found with similar actions, so that the physician must always bear in mind this phenomenon of enzyme induction when he uses several drugs simultaneously.

That barbiturates cause enzyme induction in the liver to account for their interference with coumarins is well illustrated by the experiment of administering dicumarol intravenously after pretreatment with heptobarbital.<sup>1</sup> The oral route for dicumarol is markedly affected. Here the drug is absorbed from the gastrointestinal tract, is delivered via the portal system to the liver where the increased activity of coumarin metabolizing enzymes inactivate much of the drug. After intravenous administration however the drug is almost completely bound to plasma proteins and large amounts are prevented from being rapidly inactivated by the liver.<sup>5</sup>

Anxiety is commonly present in patients who require anticoagulation therapy and consequently sedatives and tranquilizers must at times be given concomitantly. An awareness of the phenomenon of enzyme induction will greatly enhance the success of therapy in these cases, for it will encourage the physician to choose a sedative or tranquilizer from those not already shown to promote enzyme induction.

If the prothrombin activity is affected in a previously well controlled patient when a sedative or tranquilizer is added to the regimen, the possibility of stimulation of the microsomal metabolizing enzymes by this drug should be suspected. In fact, it should even be suspected that the patient has unbeknown to the physician taken a tranquilizer or a barbiturate when the physician finds a change in prothrombin activity in a patient who was previously stable at a therapeutic prothrombin activity level.

It is clear that stimulation of coumarin metabolizing enzymes by the barbiturates could make it very difficult for the unsuspecting clinician to establish smooth control of prothrombin activity by a given dose of coumarins which could lead to increased expense for the patient and loss of anti-coagulant effect.

L.H.N.

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## Anticoagulants In Cerebrovascular Disease

Both from Britain and corroborative trials in this country<sup>1</sup> it becomes clear that anticoagulant therapy offers no benefit to the patient with a completed stroke or non-embolic infarct. On the contrary the risks of cerebral hemorrhage in such patients are considerable. In the early treatment of acute cerebral infarction anticoagulants are actually dangerous because the pathological process is almost always a red or hemorrhagic infarct.

The evidence for the efficacy of anticoagulant therapy in patients suffering from transient cerebral ischemic attacks is as Pearce<sup>1</sup> points out quite inconclusive. It is true that some authors such as Sieckert et al<sup>2</sup> and Fischer<sup>3</sup> have reported what seems to be good results following the use of anticoagulants in the patient with transient cerebral ischemic attacks. On the other hand, Pearce, Gubbay and Walton<sup>4</sup> report a small but strictly controlled trial in 37 patients treated for 11 months. Fifty-nine per cent of the treated group and 45 per cent of the controls had one or more additional transient cerebral ischemic attacks. Ninety-one per cent of patient-months in the treated group and 88 per cent of patient-months in the control group were free of ischemic attacks after the trial was begun. During the period of observation one treated and two control patients developed a completed stroke.

It is apparent that there must be considerable difficulties inherent in the assessment of anticoagu-

lant drugs in patients suffering from cerebral ischemic attacks when authors disagree so radically. The question is why this should be so in this scientific era in medicine. It is a remarkable paradox that after 17 years of clinical use of anticoagulants, their value in the treatment of arterial occlusive disease is still undetermined with some publishing good results in selected cases and others no beneficial results.

Initially of course all accepted an over-simplified hypothesis on the role of clotting in arterial occlusions. The reasoning was that since arterial occlusions are sometimes thrombotic, anticoagulant drugs should be of therapeutic value. It is true that anticoagulant drugs do retard the clotting of blood in-vitro. This process however is entirely different in its genesis from intra-arterial thrombosis occurring in-vivo. Certainly blood clotting mechanisms do form a part of the process of intra-arterial thrombosis, but to what extent anticoagulants affect this process if at all is quite unknown. For example, there is now a view that the first stage in the formation of an intra-arterial thrombus is increased adhesiveness of platelets with gradual formation of a white thrombus.<sup>5</sup> This state of the platelets is not changed by anticoagulants.

A second reason for confusion is the fact that only a small proportion of patients suffering from cerebrovascular disease show evidence of thrombus in intracranial or extracranial vessels at post-mortem as shown by Hutchinson and Yates.<sup>6</sup> It is clear that the treatment of a group of such patients with anticoagulants will in fact include a large number who have no thrombus at all in their cerebral vessels. Many of these patients as demonstrated by Gunning, et al<sup>7</sup> probably have repeated episodes of micro-embolization of their cerebral vessels to account for their ischemic attacks. The influence of anticoagulants on such a process is still unknown. Such patients suffer from thrombi arising in the extra-cranial arteries.

A final reason for confusion is the likelihood that any clinically useful action of the coumarin-indanedione drugs is related to their action on blood clotting factors IX and X whereas the control of the drug dosage is commonly based upon a separate action on prothrombin and factor VII. This may explain why clotting can occur even at so-called therapeutic prothrombin levels. An important report by Ushiro and Schaller<sup>8</sup> records the presence of recent antemortem thrombi in two of four patients given anticoagulants in their trial. Apparently prolongation of prothrombin time (in the therapeutic range of both patients) is not of itself sufficient to prevent intra-arterial blood clotting.

From these and many other considerations it becomes apparent why use of anticoagulants is full of inconsistencies and illogicalities and that the use of these drugs can be justified only by the results of clinically controlled trials demonstrating a superiority which outweighs any hazards of therapy. This conservatism is justified in view of the relatively good prognosis reported in such patients provided that they are not suffering from extensive occlusive vascular disease.

Even if by more extensive trials it can be shown that any benefit accrues from anticoagulants, such an advantage would certainly be a minimal one and outweighed by complications inherent in the use of such drugs. This conservative attitude in no way denies the necessity for further investigation of thrombolytic and fibrinolytic drugs and of course the search for thrombosis in the extracranial arteries and the assessment of the role of surgery in carefully selected patients.

At the present time most physicians will concur with the conclusion of Mitchell and Schwartz<sup>9</sup> in their excellent monograph that "considered over-all, anticoagulants have proved less valuable in the management of arterial disease than was originally anticipated. What we are urgently in need of is a drug which will alter the adhesiveness of platelets to each other." One such substance, linolenic acid, was thought to have great promise in this direction but much more work needs to be done before it can finally be stated to have prophylactic value in arterial thrombotic occlusions.

L.H.N.

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## Laboratory Utilization: Use And Abuse

With the pressure of patients for admission to hospitals increasing, the hospital staffs have organized utilization committees to examine the duration of stay of each patient and how best the patient can be moved out as quickly as possible. It is probable that laboratory utilization committees will come into being to help reduce the pressure on the laboratory facilities. As Bold<sup>1</sup> points out the clinical chemistry laboratory work is increasing inexorably and his laboratory has doubled its output in the last three years. Since the work load of the clinical chemistry laboratory is increasing so rapidly, it is certainly important to discover how many of the clinical tests are really necessary.

The method Bold used to obtain answers to this question was to record all requests for clinical tests on surgical patients from August 8 to November 7, 1964. Then a randomly selected portion was followed up by asking the senior surgeon (1) why was the test done, (2) was the result considered abnormal, (3) what action was taken as a result of the test, (4) would you prefer any additional or alternative chemical test not presently available, and (5) any comments.

From the answers to the questions it was possible to classify them as follows: (1) making a firm diagnosis not possible on other grounds; supporting the clinical diagnosis; (3) non-specific; (4) useful negative; (5) progress; (6) monitoring treatment; (7) unnecessary.

The clinical details on the requisition sent to the laboratory were compared with the reason for the test as given by the senior surgeon. Over one-quarter of all requisitions were found to carry either no clinical details whatever or details which were irrelevant or inadequate. Obviously there can be no excuse for the irrelevant or inadequate clinical details on request cards. It is this which raised serious doubt in the minds of harassed laboratory staffs who often suspect that much of the work is unnecessary. Certainly there is tendency to perpetuate routine daily requests, many of which would become unnecessary if each request clearly stated the reason for the test and if each test was specifically asked for each time it was to be done and the requisition contained the reason for the request.

Most of the tests were initiated by the housemen and when the senior surgeon went over them at least 11 per cent of the tests requested were considered unnecessary. It must be admitted that because of the design of the survey, this is a minimum rather than a maximum estimate, since the surgical colleagues were placed in the position of being judges in their own case. One would have liked

to see an appreciation of the usefulness or a request by an impartial observer. The unnecessary 11 per cent is not a large proportion but it does suggest that supervision of investigations could be stricter or perhaps the senior surgeon regarded it as a price to pay for the training of junior doctors. But one is forced to inquire how much training is involved, since in the absence of clinical details on the requisition it is impossible to tell whether any of the tests needed checking or if an additional test should be performed thus possibly saving much time.

Bold points out that some of the requisitions were of a "portmanteau" nature, for example, electrolytes and urea, liver function "battery," calcium and phosphorus and alkaline phosphatase were requested somewhat indiscriminately since only one of the batch being required.

Several other conclusions are suggested by the data uncovered in the survey on laboratory chemical tests. Estimation of urine and fecal electrolytes is a valuable guide to postoperative intravenous fluid replacement and although more troublesome for ward and laboratory staff, it should replace or supplement plasma electrolyte estimations. Plasma protein estimations appeared to be of less value since over 25 per cent were considered to give non-specific information and unless clear indications are present, the helpful information likely to be gained from this test is small.

Of the tests 44 per cent were considered to provide useful negative information, but the degree of usefulness is very variable. Nearly half of the tests in this category were base-line screening such as preoperative blood urea and electrolytes and tests for metabolic abnormalities. Such a high proportion of screening tests suggests a trend in clinical medicine away from clinical judgment based on careful history and physical examination towards relying unduly on the laboratory for a diagnosis.

What is easily forgotten in all this is the patient as a person. If numerous blood tests are ordered indiscriminately and repeated daily, without a check, what can be happening to his veins, to his hematocrit, and to his sensibilities. There are documented cases in which as much as 50 to 75 ml. of blood have been drawn daily for a week or longer.

What we are witnessing is a tremendous reliance on the results of laboratory tests and an overly great emphasis on their importance. What is really required is a new outlook on the part of the house staff and attending staff. Another matter is the financial implications of the increased laboratory testing including the sizeable proportion of unnecessary testing. One is bound to ask how long can the Blue Cross or other third party afford to

finance a work load which is doubling every 3-5 years.

L.H.N.

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## Psychedelic Drugs

LSD was first synthesized in 1938 but in 1943 Hoffman discovered its hallucinogenic properties by taking it himself. A series of careful experiments by Stoll<sup>1</sup> showed that doses of as little as 30 micrograms of this agent administered by mouth to non-psychotic subjects produced autonomic changes predominantly sympathomimetic as well as kaleidoscopic visual hallucinations with intense and varying coloring hyperacusis synesthesia, tactile paresthesia, illusions, distortions of body image, feelings of estrangement and depersonalization and disturbances of mood. These occurred in the presence of unaltered orientation, critical self-judgment, and the ability to respond to interrogation by the observer. Particularly striking was the minute amount of LSD required to produce such change. The intensity of the effect of this agent differs with individuals but is proportionate to the dose. Stoll points out that tolerance develops rapidly to repeated daily doses and disappears completely three days after the medication is discontinued.

Some of the effects such as the perceptual distortions and perceptual visual illusory phenomena are not characteristic of schizophrenia. Others such as the depersonalization seen in some normal people with higher doses are strikingly similar to what may be seen in acute schizophrenic reactions. In animals large doses can produce catatonia. The subjective experiences seem to vary widely and appear related to the personality of the subject and the setting of the experience. Some describe the experience as frightening and believe they have passed through a "living hell." Others however describe their thoughts, hallucinations and sensations of depersonalization in rapturous terms.

Occasionally subjects experience overwhelming anxiety of panic proportions, rapidly alleviated by barbiturates or phenothiazines. Occasionally also prolonged psychotic episodes have been described<sup>2</sup> even though psychotic or paranoid personalities were eliminated from the study as well as those prone to the excessive use of denial. In this same study nine cases were described in whom psychiatric complications followed the unsupervised use of LSD. The subjects were seeking "consciousness expanding."

In a four month period from March to June 27, 1965, 27 patients were admitted to Bellevue Hos-

pital in New York as a consequence of ingestion of LSD and described by Frosch, et al.<sup>3</sup> There were panic reactions, reappearance of symptoms months after discontinuing the drug and extended psychoses in three who clearly had long standing schizophrenia. Each patient took the drug in anticipation of greater self-understanding. Each sought for perception and ideas and in their transcendental state believed they had achieved a resolution of their problems. Panic was rapidly replaced by a feeling of ecstasy as they felt they had achieved a new self. The trouble was that this fictional sense of self could not adjust and three schizophrenic patients withdrew from the world into catatonia and paranoia. It took over two months for two of these schizophrenic patients to become re-oriented and leave the hospital.

The belief that LSD expands consciousness and alters personality for the better has led to an increasing popularity of LSD among the lay public. Many highschool students and college students are said to take the drug ostensibly for "kicks." A large number of anxiety ridden people have begun to experiment with it in the hope of achieving help. Most often these people have taken hypnotics, stimulants and opiates before turning to LSD. This popularity may cause people to turn to it before other drugs, since LSD is believed to offer "relief with understanding" and a belief that a sustained state of improvement may be achieved. The fact is as Frosch points out, there is no evidence of any personality change for the better. Instead in some, prolonged psychoses develop, in some deterioration of personality following multiple ingestion, especially during periods of stress when to counter anxiety it is necessary to mobilize all their resources.

In reading both professional and popular literature, but scattered here and there, the lure of augmented creativity is offered and the dangers can be readily minimized by someone intent on obtaining the highly touted "positive" effects in which any resultant psychosis is pictured as readily reversible and a step towards health. In the uncontrolled setting in which LSD is used in the community, the danger of bodily injury also exists since a person under the influence of the drug may believe himself to be invulnerable to harm and take unwarranted risks, like several of Frosch's patients with panic reactions. Although no reports of prolonged adverse effects have occurred when LSD has been used as a psychotherapeutic adjunct, it is reasonable to predict that some cases of recurrence of symptoms and appearance of psychoses in previously compensated people will occur as experience with the drug grows. What is extremely important is to learn more about the physiology associated with recurrence of symptoms.



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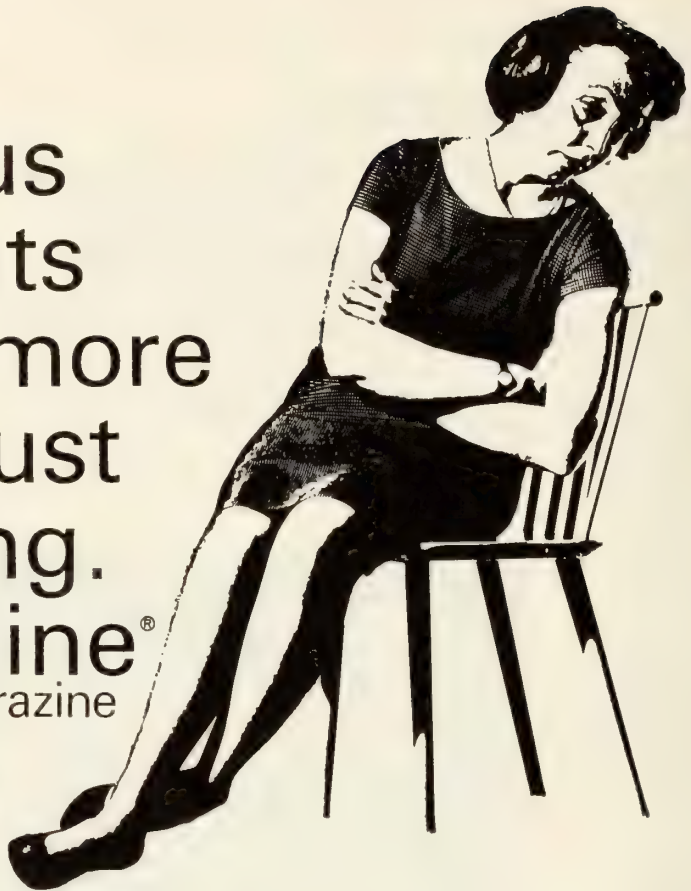
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There have been claims of great therapeutic success in the treatment of chronic alcoholism and chronic neuroses based upon experiments that did not adhere to strict scientific requirements with such extravagant pronouncements as ". . . LSD can be useful to us. It can provide us with an encounter, a new experience which will enlarge our horizon and give new meaning to life. These experiences are a part not just a therapy but of life itself."<sup>4</sup> This same kind of lure of augmented creativity is offered in some professional and popular literature. However Frosch's patients show us that all the effects are not so harmless as the enthusiasts want to believe. As a result the F.D.A. has stopped and attempted to limit the availability and use of the drug to approved research plans. Now LSD has gone underground with other hallucinogens and now an increasing illegal traffic has developed.

The promise of the good to be achieved through the psychedelic experience (mind-manifesting consciousness-expanding) is reminiscent of the optimism that accompanied the introduction of cocaine and heroin. Initially only the beneficial effects of these drugs were seen. It took more experience to recognize their undesirable properties. Similarly with LSD it is becoming apparent that the indiscriminate use of it by the general population has unfortunate sequelae. Recovery from the panic state appears to be rapid. However in a small proportion of an unselected population taking the drug in the hope of alleviating anxiety and achieving stability of personality without other therapeutic assistance more ominous effects occur such as chronic hallucinosis, severe paranoid reactions, suicide and various other psychotic developments. There is also reappearance of LSD symptoms a month to a year after the original use without re-ingestion. The New England Journal of Medicine points out that the tale of Dr. Jekyll and Mr. Hyde is prophetic of LSD in that an "unnamed powder" changed the personality of integrity of Dr. Jekyll irreversibly into his evil alter-ego.

LSD and other psychedelic drugs to come, suggest that some will be devised to have far reaching benefits upon perception, memory and mentation that may produce a new breed of man. Further work with such drugs however should be undertaken only in controlled settings by scientists capable of important critical judgment. For such psychedelic drugs are unique tools in the study of altered states of awareness, perception and ideation.

We are probably on the threshold of "well-healed" scientific inquiry into mind-memory learning, problem solving, thinking. Attempts to understand the operations of the brain must produce knowledge whose impact upon our civilization may

be immense. We must consider in advance how to deal with the ethical, political and social problems that may arise, if a real psychedelic drug comes into existence.

L.H.N.

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## Drugs Of Choice For The Emotionally Ill

Years ago medical treatment was dominated by the Hippocratic dictum to "do no harm." Now we all strive in our therapy, to "do some good." Faith and good hygiene is no longer enough and more specific and active products have replaced the "shot-gun" prescription upon which the earlier physicians relied. It is said that 90 per cent of the prescriptions written today are for compounds which did not exist twenty to thirty years ago. In all probability, considering the rate of attrition of new drugs, a similar situation will apply some twenty years hence. Most of the new drugs relate to their effect upon symptoms of anxiety and depression which are dominant in mental illness, but are also components of physical illness as well as stresses of everyday living in many people.

We not only have many new products but the products themselves may be overwhelmingly various. For example meprobamate may be prescribed "straight" under either of two trade names for at least thirteen conditions. It also has the convenience of being available under different names in a larger acting variety of these same conditions.

Aside from the various forms of meprobamate, how many psychoactive drugs are there from which the harrassed doctor may choose? A fairly recent count<sup>1</sup> shows there are thirty-three tranquilizers which one may prescribe. This total included fifteen phenothiazine derivatives, four Ranwolfia alkaloids and fourteen skeletal muscle relaxants. All these compounds in some measure tranquilize.

In addition to these compounds which assure tranquility, there are approximately thirteen drugs which activate those stricken with apathy. These are the anti-depressants which used to be called "psychic energizers." Their number can only be approximated because some of these products are short-lived. Four previously available were removed

from the market but as Smith points out, one more tenacious than the rest has returned.

With this number of compounds recommended for disorders in which diagnoses are not exact depend on clinical evaluation, it is interesting to consider what factors are most influential in determining the physician's choice of a particular compound. In an effort to determine these factors Smith asked thirty-eight psychiatric residents to express their first and second preferences for both phenothiazine derivatives and skeletal muscle relaxants. By an overwhelming vote their choices of phenothiazine were chlorpromazine and trifluoperazine HCl, and of the skeletal muscle relaxants the majority preferred chlordiazepoxide HCl. (librium) and meprobamate. How did they arrive at these choices?

Twenty-four attributed their knowledge to scientific publications. However, a survey of the literature revealed that very few results were published which specifically described the phenothiazines they preferred during their period of training. To evaluate further the influence of advertising on drug choice, it developed that twenty-seven out of thirty-four selected the drug recommended in an advertisement for this type of patient. The scientific publication on which the advertisement was based had in fact been published several years before the residents entered psychiatry! The obvious conclusion that Smith arrived at was that this group was influenced in their choice of drug by a product's presumed effectiveness and this presumption was based in turn on medical advertisement and promotion, their own results, which could not be accurately assessed, and the opinions expressed by the senior staff. If the choice of a drug for the emotionally ill is based on such unscientific evidence, what should the harassed doctor do with an out-patient who expects a drug which can relieve the patient from every variety of emotional as well as physical discomfort?

There are three categories in which the physician has drugs available to relieve though not cure: anxiety, depression, and muscle spasm. Particularly must he learn to differentiate the first two since many depressed persons exhibit much anxiety. Webster defines anxiety as "a painful uneasiness of mind respecting an impending condition occurring in nervous or mental disease as: a state of restlessness, agitation with a distressing sense of oppression about the heart" . . . synonyms given are concern, dread, fear, foreboding, misgiving, worry, solicitude, uneasiness, disquietude.

However, the physician must recognize that the state of anxiety is a normal component of the human condition in health and disease and we must not include the normal anxieties such as

precede an examination or other important event, in clinical anxiety which may be manifested in infinite ways depending on the personality and physical make up of the individual. So we have anxiety produced by an environment and anxiety of endogenous origin dependent on genetic factors, early experiences, and training. This grouping is important because anxiety caused by environmental factors may be expected to be transient and responsive to treatment, the earlier the treatment the better.

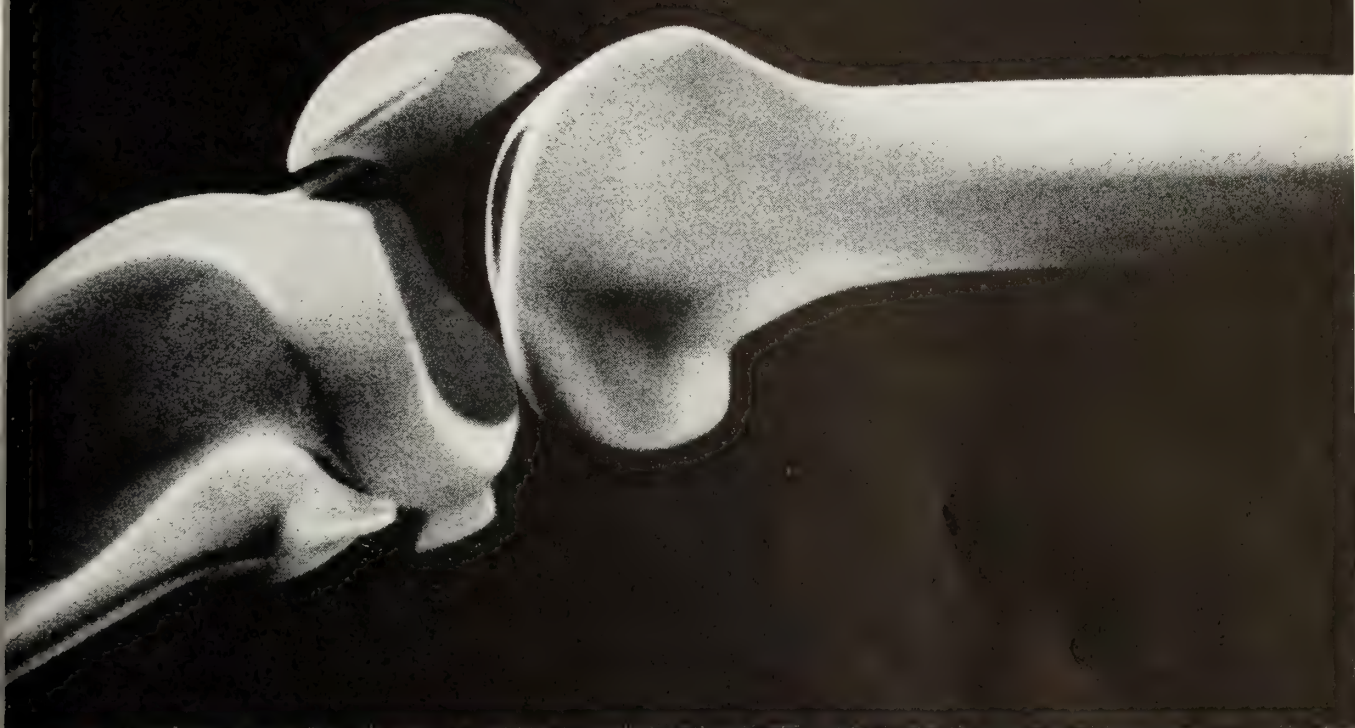
Unlike the sedatives which were readily available before chlorpromazine was introduced a decade ago, the phenothiazines do not produce too many side effects in proper dosage. They decrease the patients responses to stimuli without markedly disturbing his awareness or producing euphoria. The side effects are usually mild and transitory and are listed in detail in the descriptive literature. Many of the differences in the phenothiazine derivatives are more of interest to the pharmacologist and as Smith points out if a patient fails to improve after taking one potent tranquilizer there is little reason to have him try several other compounds with different names. The drugs in this group vary in potency but not in specificity.

Many patients whose primary illness is depressive may present overt anxiety and agitation (motor restlessness). A good clinician spending a little time in taking a history and exploring the patient's situation, past and present, can quickly recognize the true nature of the illness, can recognize depressive functioning. The family relationship, the work situation, sexual and social integration, will quickly reveal the stresses that lead to depressive feelings. The paradigm for depressive reaction is grief, following bereavement, the loss of an important person in a patient's life, the loss of opportunity, of status or of physical capacity such as occurs with the menopause or with cerebral lesion, are examples of the kinds of stress which may be associated with depressive reactions.

Much of the art of medicine consists of perceptiveness to such reactions. They may be obscured behind a facade of physical symptoms induced by autonomic disturbance. But fatigue and general lack of motivation over an extended period are probably the most common manifestations of depressive anxiety. In situational and occult depression, the anti-depressant drugs like imipramine HCl. (Tofranil) and amitriptyline HCl. (Elavil) which are not monoamine oxidase inhibitors seem the most effective, least toxic and most likely to survive.

How a physician manages an anxious patient reflects his own philosophic development. He must not reject in hostile spirit the patient with multiple non-organic complaints. Simply to order enough





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## Contraindications

Edema, danger of cardiac decompensation; history or symptoms of peptic ulcer; renal, hepatic or cardiac damage; history of drug allergy; history of blood dyscrasia. The drug should not be given when the patient is senile, or when other potent drugs are given concurrently. Large doses are contraindicated in patients with glaucoma.

## Precautions

Obtain a detailed history and a complete physical and laboratory examination, includ-

ing a blood count. The patient should be closely supervised and should be warned to report immediately fever, sore throat, or mouth lesions (symptoms of blood dyscrasia); sudden weight gain (water retention); skin reactions; black or tarry stools. Make regular blood counts. Use greater care in the elderly.

## Warning

If coumarin-type anticoagulants are given simultaneously, watch for excessive increase in prothrombin time. Pyrazole compounds may potentiate the pharmacologic action of sulfonylurea, sulfonamide-type agents and insulin. Carefully observe patients receiving such therapy.

## Adverse Reactions

The most common are nausea, edema and drug rash. Hemodilution may cause moderate fall in red cell count. The drug may reactivate a latent peptic ulcer. Infrequently, agranulocytosis, generalized allergic reaction, stomatitis, salivary gland enlargement, vertigo and languor may occur. Leukemia and leukemoid reactions have been reported but cannot definitely be attributed to the drug. Thrombocytopenic purpura and aplastic anemia may occur. Confusional states, agitation, headache, blurred vision, optic neuritis and transient hearing loss

have been reported, as have hepatitis, jaundice, and several cases of anuria and hematuria. With long-term use, reversible thyroid hyperplasia may occur infrequently.

## Dosage

The initial daily dosage in adults is 300-600 mg. daily in divided doses. In most instances, 400 mg. daily is sufficient. When improvement occurs, dosage should be decreased to the minimum effective level; this should not exceed 400 mg. daily, and is often achieved with only 100-200 mg. daily.

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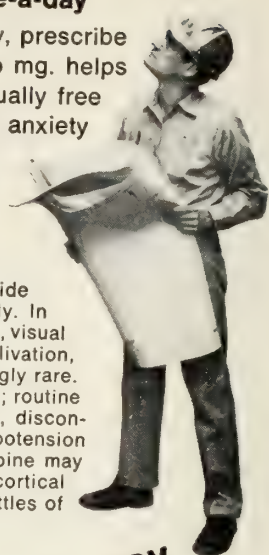
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sedative medication to mute the symptoms is contrary to the ancient Hippocratic philosophy of dedication to the patient's interest. The surgeon too can take into account the patient's need for understanding to minimize the element of fear which any illness or therapeutic process entails. If relief of emotional discomfort and suffering can be mitigated by calm explanations and personal consideration, it will work better than any drug. As Goldman<sup>2</sup> points out the use of drugs must be appropriate and judicious for the patient's long-term interest.

The conflicting views about the role of drugs in the treatment of the anxious patient as seen in the literature<sup>3,4,5</sup> indicates that we are desperately in need of careful controlled studies in this highly advertised, highly popular, but still confused field.

L.H.N.

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## The Meaning Of A Heart Attack To Some Patients

Klein, et al.<sup>1</sup> in a study of twenty patients who survived acute myocardial infarction, reveal that moderate to severe invalidism often occurs in the absence of definable physical residuals of the infarction. To these men the meaning of the heart attack was found to be predominantly concerned with fear of sudden death and fear of physical activity. We now know that a majority of men who have suffered a first attack of myocardial infarction are able to return to their work following such an attack. Why then does a significant number fail to achieve this degree of return to active living? Klein<sup>1</sup> analyzes the psychological factors in the patient and in the attending physician that bring about major failures in rehabilitation, even when the patients have recovered and the functional state of the cardiovascular system is not responsible for their invalidism.

Twelve of the twenty patients studied never returned to work following myocardial infarction. Three returned to full time at the same job as

they held before their attack. Two returned to full time at a new occupation and three at part time work. Since the physiologic basis for the invalidism was missing in these patients, the authors turned to psychological factors and the doctor-patient relationship for a possible basis of the "low" degree of recovery from the myocardial infarction. This, of course, required a study of the patients, their wives and the physicians, all of whom cooperated well.

The psychological factors in the patient that tended to reinforce invalidism were first of all their "fragility." They had fear of sudden death. They had the image of being on a "tight-rope" and any activity would throw them off. They feared activity and believed that the amount of activity would ultimately determine their fall. Activity was viewed as dangerous. Some thought the physician advised them to avoid activity. We however know that patients who wish to believe certain things will misinterpret, distort or exaggerate a physician's remarks. Thus a number of such statements concerning the dangers of activity had reference to remarks made by the attending physician at the time of the acute infarction.

Some patients and their spouses were very uncertain about the meaning of anterior wall chest pain not caused by exertion. They felt the pain portended another heart attack and some even described it as "just like another heart attack." Such pain engendered great fear and served to regulate the degree of activity. One patient after working two days awoke the next morning with anterior chest pain and "knew he had tried to do too much." The interpretation of symptoms however varied widely. One patient reported he had had "three heart attacks" while his wife thought he had seven.

The physician's response to the patient's invalidism was due both to diagnostic uncertainty about the cause of the anterior chest pain and a pattern of evaluation of symptoms in which the emotional state of the patient and his feelings were not adequately explored. Although there was a high frequency of complaints of "nervousness, anxiety, depression," the physician focused mainly on the chest pain and often felt his primary or even his sole task consisted in ascertaining whether the patient's pain was in some way physiologically related to the coronary circulation. He had to rule this out to reduce his own uncertainty when faced with a complex inexplicable symptom.

Because of the risk of sudden death and the belief that activity is inherently dangerous for the post-myocardial infarction patient, the stakes are particularly high for all physicians in this situation. The "cost" to the doctor's self-esteem is high if organic limiting factors are overlooked, and so we

find in the doctor's notes on the hospital records a preoccupation with determining the nature of the patient's chest pain and frequently almost no data or interpretation of the many other bodily symptoms or the feelings of failure, worry, nervousness, that can easily be elicited by also examining the patient's feelings.

One problem encountered in "ruling out" intermittent myocardial ischemia was related to the transient nature of the disturbance, the lack of physical findings during, as well as between the episodes. In one patient who had anterior chest pain for two to three hours everyday (strong historical evidence against angina pectoris) this diagnosis was still entertained. The lack of positive evidence for angina pectoris in the electrocardiogram taken at rest and after exercise was also thought by the physician to be of no conclusive value in the face of persistent chest pain. Thus after a history, physical examination and laboratory examination there remained considerable uncertainty in the physician's mind regarding the source of the patient's chest pain.

In the context of equivocal findings the physician exhibited two types of responses, conservatism, or avoidance of the problem altogether. If he acted conservatively he advised restriction of activity and discouraged resumption of old roles or assumption of new ones. He would say "take it easy for a while." Such a remark defined the patient's pain as related to his heart.

In situations where there was no demand by the patient for explicit answers to the question of activity levels or the meaning of the symptoms, the physician was noted to avoid the problem by saying nothing regarding these areas. He was also noted to avoid the problem by saying "do what you feel like doing," when overt concern over activity was expressed to the physician by the patient or spouse. This of course had the effect of returning to the patient the task of defining the situation. As one cardiologist stated, he was often "forced" to say to the patient "you are the only one that can decide how much you can do." This attitude was based on his belief that diagnostic techniques could not firmly establish the basis of symptoms and potential functioning, although a satisfactory exercise tolerance test leaves little room for doubt about a patient's ability to perform. In short, traditional historical criteria and exercise tolerance for the diagnosis of angina pectoris was abandoned in favor of the electrocardiogram. In turn, the negative ECG was cited as inadequate to "rule out" intermittent myocardial ischemia as a factor in the symptoms.

The observed uncertainty of the physician left no satisfactory alternative definition of the situation to

the physician, the patient or his spouse. Even though the patient reported feelings of failure, self-deprivation, and nervousness, these emotional factors were not considered as adequate explanations for the somatic symptoms and the low activity level. Klein gained the impression that physicians failed to consider these features as an explanation for the invalidism and this alternative definition of the symptom was not explored or discussed between the patient and the physician.

To improve our management of patients with myocardial infarction we must learn from Klein's studies. These include the recognition that certain features of emotional invalidism begin early in the convalescent phase and these incapacitating aspects may be avoided if the following precautions are observed. The multiple types of chest pain experienced by most patients should be explained in detail by the physician to the patient and his wife.<sup>2</sup>

Continuous appraisal of the feelings and behavior of the patient permits the physician to identify relationships between behavior and somatic symptoms.<sup>3</sup> We should realize that fear and depression are legitimate and important responses and the patient must be taught the role of these factors. The wife must be included in the discussions of symptoms particularly since over-protectiveness in the spouse may play a dominant role. Finally, graded physical activity should be a standard aspect of all phases of treatment.<sup>4,5</sup>

The suggestions in management presented by Klein, et al. can do much to decrease the incidence of post-myocardial infarction invalidism.

L.H.N.

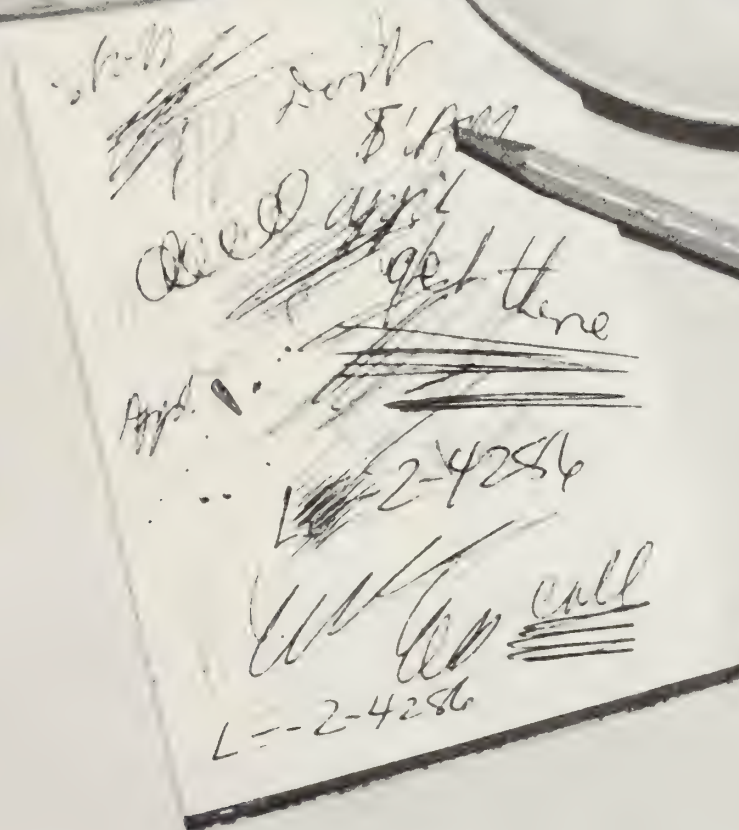
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## Dealing With The Last Chapter Of Life

In every sense, the time of death is a crisis for the patient, for his family and for the physician. The element of crisis that death holds for the patient is well recognized. He is assaulted by pain and disease. He tends to lose his dignity as a human being and feels increasing estrangement from his





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| 10%           | 63                    | 39              | 14        | 6          | 4          |
| 5%            | 30                    | 16              | 10        | 4          | 0          |

\*\* Denotes resolution of at least 50%.

\* Denotes resolution up to 50%.

### DURATION OF TREATMENT

| Number of Cases             | 14     | 24    | 18     | 14     | 9      | 3      | 7      | 4      |
|-----------------------------|--------|-------|--------|--------|--------|--------|--------|--------|
| Duration (weeks and months) | 2 wks. | 1 mo. | 2 mos. | 3 mos. | 4 mos. | 5 mos. | 6 mos. | 8 mos. |

The types of psoriasis included (parentheses indicate number of cases); Generalized (31), Palms and soles (7), Legs and feet (18), Scalp and ears (27), Groin (3), Neck (5) and Vulva (2).

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#### References:

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*Literature and samples on request.*

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family and friends. What does he do in such a situation? Will he succumb to the fear and the pain? Will he erect pathological defenses like denial, or seek revenge or attempt suicide? In spite of inevitable suffering will he be able to marshal the spiritual forces necessary to face death calmly?

The family's crisis is more varied. They must stand by the patient at the end of life giving him support despite their own suffering. After death the family must come to grips with the shock of the loss and the need to express grief. Finally through successful mourning the members must regroup and face the world renewed.

The physician's crisis in a patient's death is perhaps the most complex, for not only must he make certain that everything possible has been done to save the life, but if this is not possible, then he must manage to help the patient achieve the most peaceful death possible and also help the family go through each of its crises successfully.

The key to success in managing the crises of death lies in the physician's own attitude. He must stop and do some hard thinking about himself for sooner or later he also will face the same fate as that of the patient he is trying to help. Will his final illness be a hopeless and dismal experience or will he "overcome" it in spite of the inevitable suffering? How should we all prepare ourselves for the great adventure? Having answered that question we can be of some help to our patients.

First of all, the physician must make sure that everything that may reasonably be done to effect a cure and make the patient as free of pain as possible has been done. Just as in any clinical situation he has the obligation as far as the patient's resources will permit to procure for him the services of any facility or any consultant which he might want for himself were he in the same predicament. Once the optimal physical measures have been carried out, the physician's role is to help the patient and the family to deal with the outcome, good or bad, despite the difficulty of maintaining his efforts in an increasingly discouraging situation.

The physician's classic role in society is that of a responsible person to whom the patient can turn with trust and confidence for advice as well as technical help. This role does not call for heroic measures and frantic maneuvers once hope is lost, and the physician then need not feel defeated when death supervenes.

In most instances the physician and the patient have advance warning that death is approaching. Such a warning will have varying degrees of certainty as regards time. Whatever the situation, however, the physician must resolve the enigmatic

problem. How to inform the patient of the grim situation without injuring him? The physician to be sure must tell the patient the facts of his physical condition as fully as the patient wishes to know them, but always with a liberal admixture of understanding and hope. Many patients will make it clear that they do not want to be told the whole truth whether they say it in as many words or not and of course their wishes must be respected. The family however will almost invariably want to know. The physician can put his information at their disposal, but once the information has been provided, there is no need of repeating it.

As the time of death approaches the patient is beset by feelings of loneliness and estrangement as well as by apprehension about the future and by the ravages of his illness. Naturally the physician will deal with the latter in a direct and effective fashion. For the loneliness and apprehension he can truly set a model for the family to follow. He must avoid the dangers of over solicitousness and also of false reassurances, for everything "isn't all right." Neither is everything lost. He can help the patient to realize what is possible and what is not.

The physician can instruct the family not to give way to excessive emotional displays in the presence of the patient. On the other hand, the patient will welcome signs of legitimate concern on the part of the family. Like the physician whom they can imitate, they should be realistic and concerned in their approach thereby enabling themselves to render the strongest support to the patient. They may also be encouraged to call upon their minister who can provide immeasurable comfort in the lonely hours that precede death.

In this age of technical advances no one is more thoroughly familiar with the elaborate techniques not only for diagnosing and treating disease but for prolonged life than is the doctor. Especially in dealing with patients having metastatic cancer, the old ghostly questions almost invariably come up. Why was it not discovered in time? If only an operation had been done earlier this may not have happened. Why did it happen to me, etc. etc. The feelings of resentment and guilt which prompt such expressed and silent thoughts are terribly tormenting and cannot be ignored. The physician must point out that in an extremely difficult situation one inevitably looks back but there is no use to affix blame. Regardless of what has gone before the situation is there to be faced and the past must be put behind them. From this moment on the physician should be unyielding in his decision not to listen to hindsight, wanderings and recriminations, and he must warn the family regarding well

meaning friends whose unsolicited and unreliable advice may provoke panic stricken relatives into spending large amounts of money and time in fruitless visits to other clinics and other physicians.

Modern medicine's startling armamentarium for prolonging life makes the problem of interfering with "death from natural causes" extremely difficult. Do we have the right to interfere significantly with the termination of physiological processes in a person who seemingly has a hopeless illness and who is a burden to himself as well as his family? As physicians do we have the obligation always to prolong life with every means at our disposal. In a young person whose mind is still active the decision is easy. With older persons in the twilight of life it is more difficult. It is the physician's duty however to use his wisdom and clinical judgment in recommending that the family utilize all the techniques of modern medicine as far as these are likely to be helpful and effective but to abstain from these recommendations when the time of effectiveness is past.

Once death has occurred the family is in a state of emotional shock, whether from sudden and unexpected loss, from relief of prolonged agony or from grief. At this time too the physician is tired and saddened. It is exactly at this point however that it becomes his burden not to turn away and seek his own peace but to turn toward the family. He needs to explain to them what has happened in simple and sympathetic words and to give them the opportunity of easing their own suffering. Almost every family needs reassurance at this time that everything was done, that they did everything they could, that the patient's suffering was minimal and that for him it is well that it is now over.

Depending on the family, they usually need to work with the physician, to complain or to obtain reassurance and support. A minimum of a few minutes spent in this constructive effort can provide a suitable conclusion to the management of the crisis of death and can turn the family towards their job of reestablishing new integrity and working towards their future. This will cement the rapport between family and doctor for future cooperation.

Sir William Jenner has summed up the essential qualities for the medical man that will see him through the difficult time of crisis. . . . "He must be honest, he must be dogmatic, he must be kind."

L.H.N.

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## Mutual Medical-Dental Problems: Prevention Of Subacute Bacterial Endocarditis Associated With Dental Procedures

Until recently our concept about subacute bacterial endocarditis was that it occurs most frequently in individuals with rheumatic heart disease, congenital heart disease, and syphilitic aortic valvular disease. In all such patients we have been alert to the danger imposed by dental manipulations. However, normal heart valves can also be the site for the development of endocarditis especially in patients over 60 years of age. Anderson<sup>1</sup> studied the clinical features of 14 patients who developed bacterial endocarditis over the age of 60 and found that in only two of these patients was there any known antecedent valvular disease. He pointed out that this disease can occur in patients whom we do not expect to become affected and may run a more insidious clinical course than it does in younger patients.

Guze and Pearce<sup>2</sup> studied 17 patients who acquired bacterial endocarditis during hospitalization. The median age for this group was 59 years and the primary illness which required hospitalization was a condition requiring an operation. It was a post-operative infection which was thought to be etiologically related to the subsequent valvular infection. Here again the endocarditis occurred most frequently on normal valves. It is known that verrucous vegetations, non-infected, can occur on heart valves in animals following stressful situations, and it may be this situation occurs in man, as Angrist postulated, and if a nidus so formed becomes infected with streptococcus from the blood stream, then subacute bacterial endocarditis ensues. Since all patients over the age 60 are, when undergoing an operation, susceptible to the development of bacterial endocarditis, it seems reasonable that they also should receive prophylactic therapy to avoid this dangerous complication.

It is recognized that from 50-80 per cent of patients develop bacteremia during dental extractions of extensive dental procedures especially in the presence of badly infected gums and the most common organism noted and the organism which causes the overwhelming majority of cases of subacute bacterial endocarditis is streptococcus viridans.<sup>3</sup>

The recommendation of the American Heart Association to prevent septicemia due to streptococcus viridans and the resultant bacterial endocarditis is based upon the assumption that the patient's gums and mouth is populated by strains of streptococcus viridans which are sensitive to



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penicillin. Thus it is recommended that penicillin administration be begun several days before the procedure is optional, and 500,000 units of buffered penicillin G or phenoxymethylpenicillin is to be given orally four times daily and continued for two days after the operation. An alternative course is to give an intravenous injection of procain penicillin supplemented by 600,000 units of crystalline penicillin one to two hours before the procedure. Then for the next two days 600,000 units procain penicillin are given intramuscularly. However, if the patient is allergic to penicillin, then erythromycin is to be used.

An important development in bacteriology in recent years requires a re-evaluation of our current practices in prophylaxis against subacute bacterial endocarditis. This is the recognition of penicillin resistant strains of alpha streptococcus (viridans) in the gums and saliva of patients who are to undergo tooth extractions or periodontal manipulations. Many such patients are on penicillin prophylaxis for rheumatic heart disease and such treatment with penicillin can definitely alter the bacterial flora of the mouth and promote the emergence of gram negative organisms as well as penicillin resistant streptococcus viridans.

Garrod and Waterworth<sup>4</sup> reported two cases of bacterial endocarditis due to penicillin resistant streptococcus viridans in which dental extraction was preceded by prophylaxis penicillin therapy. They also noted that in 31 patients on penicillin prophylaxis for rheumatic fever, the vast majority of strains of streptococcus viridans isolated from the saliva were resistant to penicillin. They also noted that in 2 normal adults given phenoxymethylpenicillin 250 mg four times daily, that a population of resistant alpha streptococcus was established within 48 hours.

There is normally present in the mouth of patients 4.3 per cent resistant alpha streptococcus. However, after penicillin has destroyed the sensitive strains, the resistant strains become dominant. Thus Naiman and Barrow<sup>5</sup> cultured the anterior gum-tooth margins and the posterior pharynx in 21 children receiving penicillin prophylaxis for rheumatic fever and found 81 per cent of cases studied were now implanted with penicillin resistant alpha streptococcus. Gould and Sperber<sup>6</sup> realize that the question of treating all patients undergoing surgery over the age 60 prophylactically to prevent bacterial endocarditis is still controversial. Further statistical studies are necessary to determine whether the percentage of cases of bacterial endocarditis found in the 60 or over group after operation is high enough to warrant a treatment which in itself carries a small risk.

On the basis of the evidence presented above Gould and Sperber suggest a rational plan for therapy to prevent bacterial endocarditis. It takes into account three factors. One is that penicillin administration quickly leads to penicillin resistant alpha streptococcus populating the gums and mouth of patients. The other is that it takes at least a week for such resistant strains of streptococci to disappear after penicillin prophylaxis is discontinued. The third is that many patients may be allergic to penicillin altogether and require a different antibiotic to prevent bacteremia and subacute bacterial endocarditis after dental procedures.

Their suggested plan is that patients who are on oral penicillin prophylaxis for rheumatic heart disease, should discontinue this medication for at least one week and then institute either a parenteral form of prophylaxis on the day of the contemplated operation or an alternate mode of treatment by giving an antibiotic such as erythromycin orally 250 mg QID for 3 days beginning 6 hours prior to dental surgery or instrumentation.

The patients prone to develop subacute bacterial endocarditis after dental manipulation such as those suffering from rheumatic heart disease, congenital heart disease and syphilitic aortic valvular disease, who are not on penicillin prophylaxis and are not allergic to penicillin, can receive penicillin as follows: 1-2 hours before the procedure as outlined in the alternative program of the American Heart Association, the patient should receive intramuscular 600,000 units of aqueous procaine penicillin with 600,000 units of aqueous crystalline penicillin. Thereafter daily for 2 days they should receive 600,000 units of aqueous procaine penicillin intramuscularly.

It must be recognized however that even though the post-operative dental phase of septicemia will be controlled by the penicillin, since it is assumed the invading organism is sensitive to penicillin, nevertheless studies that will compare this method with the alternate method of using a different antibiotic may reveal that erythromycin is equally as effective in preventing subacute bacterial endocarditis and will not produce a population of penicillin resistant streptococci in the mouth.

L.H.N.

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## Screening Blood Donors For Hepatitis Virus

One of the least desirable results of blood transfusion is the transmission of hepatitis virus to the recipient. Allen and Sayman<sup>1</sup> pointed out the substantial mortality from this type of hepatitis, particularly in patients over 40 (23 per cent in their series). It would seem most desirable to find a simple and practical test of donor blood which would permit exclusion of hepatitis carriers. The use of "batteries" of liver function tests is extremely impractical as almost 30 per cent of healthy blood donors have one or more abnormal tests.<sup>2</sup>

In 1959 Bang et al<sup>3</sup> proposed the use of SGOT levels as a practical test. They found that if the SGOT was below 40 units only 1.5 per cent of recipients developed hepatitis whereas if the level was over 100 units 5.5 per cent of recipients were afflicted. There were many flaws in this article, most of them pointed out by Brandt and coworkers.<sup>4</sup> They write "On the basis of our study we have concluded that the capacity of routine determinations of transaminase activity to prevent post-transfusion hepatitis is low in the Netherlands—." Brandt evaluated both SGOT and SGPT in this regard.

Still more recently Sussman and Sherman<sup>5</sup> studied the activated partial thromboplastin test as a screening test for carriers of hepatitis virus. Among 5539 donors there were 311 who demonstrated a prolonged PTT. There were 5 suspect carriers in this group of 311, and 5 more among the remaining 4977, indicating a 16 to 1 chance of finding a carrier in the group with abnormal findings. By this technique 5.5 per cent of all donors would be discarded to eliminate 50 per cent of the carriers. Put another way, 306 of the 311 units would have been wasted to eliminate the 5 carriers. It is apparent that this is not a practical or reasonable procedure and that the search for a screening test must still go on.

There are several reasons why such a search is extremely difficult and may not finally succeed until the virus itself can be isolated readily. One

reason is that the index of infectivity of donor blood is the occurrence of hepatitis in the recipient. Inasmuch as some recipients die during the incubation period and others are immune by virtue of prior infection this is a poor index. Probably 1 in 200 donors is a carrier<sup>6</sup> so that Sussman and Sherman should have found 27 rather than 10 carriers. The difference is accounted for chiefly by recipient death and immunity. A second reason is that most carriers do not exhibit any overt manifestations of hepatitis. Some of these persons remain carriers for 1 to 5 years with no evidence of disease.

In conclusion none of the laboratory tests yet proposed and studied provide a reasonable method of excluding carriers of hepatitis from serving as blood donors. Aside from exclusion by history and physical examination of persons with obvious hepatitis the only way of limiting blood-borne hepatitis is by restriction of transfusion to patients whose condition demands this treatment.

R.B.

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A supply of auto emblems, bearing the insignia of The Connecticut State Medical Society, is kept on hand at all times at the headquarters offices at 160 St. Ronan Street, New Haven, Connecticut. The price of each emblem is \$5.00 postpaid.



## Meet Our Editor

Dear Dr. Richards:

*... I must once again express my amazement at the contributions made monthly by Louis Nahum. All of them deserve widespread dissemination. How one man can write on such a wide range of subjects is a source of wonder. Each carefully presented editorial makes me look forward to receiving every single issue of CONNECTICUT MEDICINE. I do think you must be very happy to serve as managing editor of a Journal that has as its editor, Dr. Nahum. Don't you think it's about time you carried his photo in the magazine? I would like to see what he looks like. ...*

Cordially,

CARL BEARSE, M.D., Editor  
Massachusetts Physician

*The Business Manager is more than pleased to comply with Dr. Bearse's request.*

### About Dr. Nahum

Louis H. Nahum, New Haven, was named Literary Editor of CONNECTICUT MEDICINE in June, 1958, and, in May, 1962, was appointed its Editor with full responsibility for the editorial content and the quality of all scientific articles that appear in the *Journal*. Working with the publication's Editorial Committee, Dr. Nahum seeks to maintain the interest of member physicians by keeping them informed on the recent developments in medical

science, presenting scientific material of general interest and devoting space to expressing the views and policies of the Connecticut State Medical Society. This dual purpose makes his work a real challenge.

Dr. Nahum's dedication to research and to its proper dissemination dates back to his 1929 paper on brain fuel, prepared in collaboration with Dr. Harold Himwich, and read at the International Congress of Physiology in Boston that year. Some of his editorials that have drawn enthusiastic response are "Hypothesis or Conclusion," "Preconceptions and Scientific Progress," "Pain and Suffering," "Nuclear Medicine," "Sixty-Five and Over," "Smoking and Thrombosis," and the series, "Report" and "Science Tools."

Dr. Nahum graduated from the Yale Sheffield Scientific School in 1912 and from the Yale Medical School in 1916.

He is a Fellow of the Council on Clinical Cardiology, American Heart Association and a Diplomate of the American Board of Internal Medicine; lecturer emeritus in physiology, Yale University School of Medicine; consultant in medicine, Hospital of St. Raphael and Yale-New Haven Medical Center, New Haven; Griffin Hospital, Derby; Middlesex Hospital, Middletown; and attending in cardiology, Milford Hospital, Milford.

He is engaged in the private practice of internal medicine and cardiology in New Haven.



# Laboratory – Clinician – Laboratory Feedback

Roy N. Barnett, M.D.

■ A recent and illuminating article by VanPeenen and Lindberg<sup>1</sup> illustrates a most important point; clinical laboratory tests must be oriented to patients and do not exist in a vacuum.

At the University of Missouri the authors supervise a highly automated and computerized laboratory. All of the usual "Quality Control" methods to assure accuracy and precision of results are used. On a certain date a defective new lithium nitrate reagent was introduced and for the next 2 weeks the reported sodium values were about 5-6 mEq/L lower than the true values. None of the "Quality Control" techniques gave a clear indication of this consistent error. The error was discovered and traced down when the astute clinicians pointed out that the clinical state of their patients was not compatible with the low sodium values reported. At this point the defective reagent was discovered and it was possible to trace the length of time that it had been in use.

Clinical laboratory values are only part of the knowledge which a good physician possesses about his patient. The blind faith which some unwary practitioners place in test results, even when they run completely contrary to the whole clinical state, is a cause of great concern to clinical pathologists. Whenever one or more laboratory results do not fit with the other data the attending physician should make every attempt to clarify the situation, including conferring with the laboratory director. Sometimes this will point up the existence of an unsuspected problem in laboratory analyses, thereby benefitting many additional patients.

Quality control systems should detect systematic errors. Why did they fail Lindberg and VanPeenen? It should be realized that such systems depend on knowledge of the inherent variability of the determination. In the particular instance quoted the inherent variability of the sodium method was great, indicated by a Standard Deviation of 3 mEq/L. (This means that if true value was 140, reported value would be between 134 and 146 in 95 per cent of analyses. Most laboratories can analyze serum sodium more precisely, with an SD of 1 to 2 mEq). The greater the variability the wider the range for the Quality Control system and the more difficult it is to detect systematic errors. Many of our clinical laboratory tests are not nearly as reproducible as would be desirable, and new methods are urgently needed.

Random errors, resulting from a wide variety of mishaps, mislabellings, misplaced decimal points, etc. are regrettably common. Estimates of their frequency range from 1 in a 100 to 1 in a 1000 tests. No one but the clinician can possibly detect most of these. (Clinical laboratories are not unique in respect to random errors. Think how many "space" experiments have failed despite the most elaborate and expensive checks and controls!)

One further facet of the problem is automation. The phrase "automated laboratory" brings to mind an inhuman degree of perfection with elimination of random and systematic errors. The computers' word "GIGO" is particularly appropriate here. It means "Garbage In, Garbage Out". Many of the methods presently used by "automated laboratories" can be considered "Garbage" because of their inherent lack of precision. They are certainly cheap and efficient, but unless they furnish the desired information they are useless. The greatest danger of mass screening by such technique is the loss of the "feedback" which helps hospital laboratories so much. If 1000 normal people are screened and the 1 abnormal value missed the whole system has failed to provide the "early diagnosis" for which it was established. Yet the laboratory would never know that this 1 patient has been missed.

To summarize the lessons from this stimulating article.

1. Most quantitative techniques presently used in clinical laboratories are still less accurate than is desirable.
2. In detecting random and even systematic errors in laboratory tests the clinician who knows his patients and their physiology is in a particularly favorable position.
3. A constant feedback between laboratory and clinician is essential to provide the best quality of laboratory work.

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DR. ROY N. BARNETT, Director of Laboratories, Norwalk Hospital and Associate Clinical Professor of Pathology, Yale University School of Medicine, New Haven, Conn.

# Vocal Cord Paralysis – Symptoms And Treatment

Robert S. Rosnagle, M.D.

■ Paralysis of the laryngeal musculature is a common but often misunderstood affliction. The misunderstanding lies in the variety of vocal symptoms which this paralysis can produce. These symptoms depend largely on the position of the paralyzed vocal cord and even that can change with time. Accurate diagnosis and treatment of this paralysis demands inspection of the vocal cords. This can usually be accomplished using indirect (mirror) laryngoscopy in the office. Further confirmation of the findings may require direct laryngoscopy. Rehabilitation of the patient often requires surgical intervention on the larynx.

## Positions Of The Paralyzed Vocal Cord

The normal vocal cord moves to the midline during phonation and then abducts to provide an open airway for respiration. In the position of abduction, phonation is not possible, while adequate inhalation is not possible when both cords meet in the midline. Paralysis can fix the vocal cord either in extreme abduction or adduction, or at some midway point. A point just slightly away from the midline is the most common site of a paralyzed vocal cord—the paramedian position.

With unilateral cord paralysis no impairment in breathing will occur and the voice will remain quite normal so long as good cord apposition can be achieved by the one mobile vocal cord. However, if the paralyzed cord fixes in a more lateral position, the quality of the voice will be diminished in proportion to the distance of the cord from the midline. The paramedian position produces a voice which is "breathy." The patient cannot speak loudly and can utter only a few syllables before stopping for another breath. Figure I illustrates the principal positions of the paralyzed vocal cord.

Bilateral vocal cord paralysis as the result of bilateral recurrent laryngeal nerve impairment occasionally produces the dramatic picture of acute airway obstruction. In this situation both cords are fixed in the midline, unable to abduct. Emergency tracheotomy is necessary to provide a patent airway. The only voice abnormality in this instance may

be a loss of timbre and some reduction in range. To many ears the voice may sound normal. The real problem is the inability of the patient to be freed of the tracheotomy tube. This situation may also develop insidiously over a long period of time.

Both the physician and the patient may be unaware of vocal cord pathology, so long as the voice remains satisfactory. With the loss of normal phonation however, both the physician and the patient may seek the cause. It is at this point that laryngoscopy is often first employed and the diagnosis of vocal cord paralysis is finally made.

## Treatment

Bilateral midline vocal cord paralysis usually requires compromise between the surgeon and the patient. A good voice (which the patient wants) must often be sacrificed to provide a functional

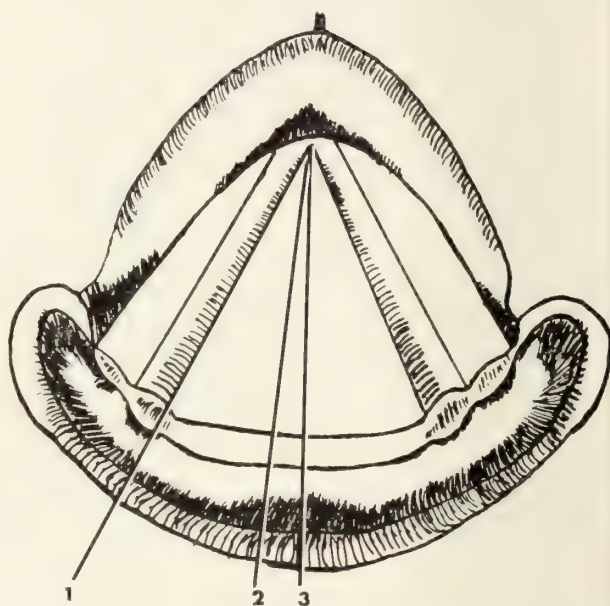


FIGURE I

Positions of the paralyzed vocal cord.

1. Extreme abduction—phonation is difficult.
2. Paramedian position—the most common site; this produces a hoarse, breathy voice.
3. Mid-line—good phonation. If bilateral, respiration is severely impaired.

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*Supported by grants from the American Cancer Society No. ACST-267A and U.S. Public Health Service No. USP-NB-0546502.*

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FIGURE II

Low power view (4X) of a human larynx cut in the frontal plane. Note the atrophy of the paralyzed left vocal cord (V) as compared to the right vocal cord.

airway (which the surgeon wants). The classic King-Seed operation<sup>1</sup> draws one paralyzed vocal cord away from the midline and fixes it in a lateral position. Thereafter the patient has an adequate airway, but a husky voice. Another solution to this problem is the Tucker one-way valve, placed in a standard tracheotomy tube. Air can be inhaled through the tube in the usual manner. The valve then closes and exhaled air passes out through the larynx, permitting phonation. Although this device leaves the patient with his normal voice and provides an adequate airway, it has the disadvantages of being mechanical and of removing an element of airway protection. Many patients decide that they would gladly sacrifice vocal quality to be rid of the nuisance and care of the tracheotomy tube.

Until recently, unilateral vocal cord paralysis with the cord in abduction was left untreated because no satisfactory method of treatment was available. A simple solution is obvious: the paralyzed cord can be returned to the midline. It can lie there without significant obstruction to the airway and its presence in the midline, even passively, allows a point of apposition for the active cord and permits nearly normal phonation. Surgical attempts at such correction have never been popular, partly because of their difficulty and



FIGURE III

A more posterior view of the same larynx seen in Figure II. Teflon (T) has been injected into the region of the paralyzed vocalis muscle, increasing the bulk of the vocal cord.

partly because of their almost uniform failure. In 1912, Brünings<sup>2</sup> successfully injected paraffin into such paralyzed vocal cords with lasting voice improvement in most cases. In spite of Brünings' success, little use was made of this technique. In 1955, Arnold<sup>3</sup> reported on the successful use of diced autogenous septal cartilage to augment paralyzed vocal cords. From this successful, but technically difficult method, Arnold<sup>4</sup> and Lewy<sup>5</sup> have developed a technique employing inert material which is easy to use, does not migrate, and produces few reactions.

### Procedure

Powdered Teflon, supplied by the Ethicon Company as a sterile 50 per cent w/v suspension in glycerin, is injected into the area of the vocalis muscle on the paralyzed side. Visualization for the procedure is obtained through a direct laryngoscope held in place by a Lewy chest support. The procedure is carried out under local anesthesia. Approximately 0.5 cc of the material is usually sufficient to reposition the cord. In most instances a distinct improvement in the voice can be noted at the operating table and actually serves as the end point of the injection. The patient is observed in the hospital for 2 to 3 days, after which he is able to resume normal activities. Usually the permanent voice will mature within 7 to 10 days after the injection. If breathiness is still a problem, more Teflon can be injected.

Complications can occur but are rare if proper precautions are taken. Over-injection may result in airway compromise. Inflammation and edema—usually the result of superficial injection—and loss of Teflon due to mucosal tears are often experienced before the technique is completely mastered.

The vocal improvement resulting from this procedure lasts indefinitely in most patients. The accompanying slides are part of a serial study made of a larynx into which Teflon had been injected 13 months prior to death.\* The Teflon shows no remarkable evidence of migration. Microscopic examination reveals evidence of fine capillaries and fibroblasts. A few foreign body giant cells are seen among the masses of foreign granules. (Figures 2 and 3). No studies yet extend beyond a 3 year period, so that long-term effects are unknown.

One patient in the series of the Yale-New Haven Medical Center experienced acute regression of his vocal quality following bronchoscopy performed about 6 weeks after Teflon injection. We believe that the pressure of the bronchoscope in the larynx may have compressed the injected cord, bringing a decrease in its bulk. No other patient here has shown such regression.

### Application

This type of augmentation is obviously useful only in specific cases of vocal cord paralysis. It should not be used in patients who have hysterical dysphonias or in patients who have not had proven paralysis of at least 6 months, since either condition may be reversible by non-surgical means. It is of no value in ordinary cases of bilateral vocal cord paralysis since maintenance of an adequate airway depends on at least one mobile vocal cord. The method has been used successfully to augment vocal cords scarred by surgery or trauma. It can be used in selected cases of neurologic disease resulting in unilateral vocal cord paralysis.

In addition to vocal improvement, certain other functions are improved by restoring glottic com-

petence. The ability to cough is improved—particularly valuable in patients whose paralysis may be the by-product of thoracic surgical procedures. Temporary improvement in glottic function has been achieved by injecting only glycerine into patients in the period immediately following surgery where a recurrent laryngeal nerve is known to have been traumatized or sacrificed.<sup>6</sup> In such patients the procedure can be done at the bedside, using indirect laryngoscopy. The benefit in these cases lasts only for the few days until the glycerine is absorbed. Permanent injection can be performed at a later date, if desired. The Valsalva maneuver is also improved when glottic competence is restored. This is particularly useful to men who do heavy lifting. It also reduces the likelihood of fecal impactions. Thus, the procedure may be applied in certain cases where vocal improvement is not the main objective. In all instances laryngeal function is improved without any period of serious debilitation.

### Summary

Vocal cord paralysis is not easily categorized because it can produce many different symptoms. Visualization of the cords is necessary for accurate diagnosis. Correction of the defects caused by paralysis is possible and good function can be restored in most cases.

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\* The serial sections were done as part of the research program of the Otolaryngology Research Laboratory, Yale University School of Medicine. The larynx was obtained from Dr. Robert Lewy of Chicago, Illinois.



# Cerebrospinal Fluid Lactic Acid Dehydrogenase Diagnostic Significance In Neurologic Disorders

Joseph A. Glennon, M.D. and Mary K. Healy

■ The enzyme lactic acid dehydrogenase (LDH) has been studied in cerebrospinal fluid (CSF) in a number of neurologic disorders with conflicting results.<sup>1-11</sup> In this study, the LDH activity in CSF of normal patients and in that of patients with a variety of neurologic diseases was examined.

## Materials And Methods

The patients included were seen at Hartford Hospital or Newington Veterans Administration Hospital. CSF specimens were obtained by the usual method of lumbar puncture and ventricular fluid from several patients by aspiration at the time of operation.

The patients designated as normals had no history or physical findings suggesting a neurologic disorder and their CSF specimens were normal. The diagnoses in patients with disease were based on pathologic interpretation of biopsy or autopsy material when possible or combined clinical and laboratory examination.

Determinations of LDH activity were performed at Hartford Hospital by the same technician. Specimens were centrifuged to remove cellular elements, and stored at 4°C until enzyme activity was measured. This was performed within 72 hours in the majority of cases and no later than 1 week. Blood contaminated specimens were discarded with the exception of those related directly to the neurologic condition (e.g., subarachnoid hemorrhage).

Protein concentration, cellular elements and chemical analyses of specimens were measured in the usual manner for this laboratory. The sulfosalicylic acid method was used to determine protein concentration.

A full description of the method used to measure LDH activity is presented elsewhere.<sup>12</sup> It is based on the methods of Hill,<sup>13</sup> Wroblewski and La Due<sup>14</sup> and Henry, Chiamori and Golub.<sup>15</sup> Tris buffer was used, pH was adjusted to  $7.45 \pm 0.05$  and the reaction of pyruvate to lactate was utilized. 0.2 ml specimens of CSF were analyzed by this spectrophotometric assay; the LDH activity was expressed in terms of absorbance units. One unit of activity

equalled a decrease in absorbance of 0.001 per minute per ml of CSF at 37.5°C.

## Results

### Normal Subjects:

CSF LDH activity was measured in 175 normal subjects (111 males). The oldest was 87 years and the youngest 4 months with an average age of 49.8 years. The overall range of CSF LDH was 10-76 units with a mean of  $40.0 \pm 17.4$  S.D.\* units.

Statistical analysis showed a significant ( $p < .01$ ) correlation between LDH activity and age in normal males with activity increasing as age increased (equation for regression line— $Y = 42.39 + 2.18x$ ). The correlation was not significant in normal females ( $p > .05$ ). If male values were corrected for the influence of age the correction ranged from +12 to -8 units at the extremes of age studied.

No correlation between cell counts, CSF sugar or chloride concentration and LDH activity was noted in these normal subjects. Comparison between protein, age and LDH activity respectively was not made because of the grossness of the sulfosalicylic acid method for determining protein concentration.

## Neurologic Disorders

LDH activity was measured prior to any treatment or procedure unless stated otherwise. An elevated activity was one greater than 75 units (normal mean + 2 S.D.). The values are presented in Tables 1-6.

### Neoplasms:

There were 18 patients with primary and 20 with metastatic intracranial neoplasms (Table 1). The diagnoses were established by pathologic examination of surgical or autopsy specimens. CSF LDH was elevated in 7 of 18 patients with primary and 6 of 20 with metastatic neoplasm of the brain.

From the Departments of Medicine, Hartford Hospital, Hartford, Connecticut, and Newington Veterans Administration Hospital, Newington, Connecticut.

\* Standard deviation.

DR. JOSEPH A. GLENNON, instructor, department of medicine, University of Wisconsin Medical School, Madison, Wisconsin.

MARY K. HEALY, technician, clinical chemistry laboratory, Hartford Hospital, Hartford, Conn.

TABLE I  
INTRACRANIAL NEOPLASMS

| HISTOLOGIC TYPE          | PRIMARY |             |                             | METASTATIC                 |     |             |                              |
|--------------------------|---------|-------------|-----------------------------|----------------------------|-----|-------------|------------------------------|
|                          | AGE     | SEX         | IDH                         | PRIMARY SITE               | AGE | SEX         | IDH                          |
|                          |         |             | ACTIVITY<br>(UNITS)         |                            |     |             | ACTIVITY<br>(UNITS)          |
| Astrocytoma              | 48      | M           | 34                          | Lung                       | 36  | F           | 56                           |
| "                        | 69      | M           | 18                          | "                          | 51  | F           | 32                           |
| "                        | 8       | F           | 60                          | "                          | 67  | M           | 59                           |
| "                        | 39      | M           | 64                          | "                          | 46* | M           | 220                          |
| "                        | 70*     | F           | 76                          | "                          | 68* | M           | 247                          |
| "                        | 51      | M           | 40                          | "                          | 66  | M           | 20                           |
| "                        | 7*      | M           | 201                         | "                          | 65  | M           | 36                           |
| Glioblastoma             | 46      | M           | 26                          | "                          | 69  | M           | 47                           |
| Multiforme               | 62*     | M           | 83                          | "                          | 60  | M           | 69                           |
| "                        | 58      | M           | 57                          | "                          | 48  | M           | 44                           |
| Acoustic Neuroma         | 53      | M           | 55                          | "                          | 65  | M           | 68                           |
| "                        | 37      | F           | 44                          | Breast                     | 47* | F           | 101                          |
| Hemangioblastoma         | 50      | M           | 25                          | "                          | 69* | F           | 580                          |
| Oligodendroglioma        | 50*     | F           | 78                          | "                          | 55  | F           | 42                           |
| Chromophobe adenoma      | 42*     | F           | 172                         | "                          | 60  | F           | 65                           |
| with hemorrhage          |         |             |                             | Larynx                     | 47  | M           | 46                           |
| Meningioma               | 46      | M           | 52                          | "                          | 50* | M           | 93                           |
| Sarcoma                  | 62*     | F           | 176                         | Malignant Melanoma         | 42  | F           | 30                           |
| Choroid plexus papilloma | 3 mos*  | F           | 160                         | Large Bowel                | 68  | M           | 64                           |
|                          |         |             |                             | Chronic lymphatic leukemia | 64* | M           | 308                          |
| Total 18                 |         | 11 M<br>7 F | Mean 78.9<br>Range (18-201) | Total 20                   |     | 13 M<br>7 F | Mean 111.5<br>Range (20-580) |

\* Elevated LDH Activity (i.e. > 75 units).

Ventricular aspiration was performed in 4 patients with intracranial neoplasm associated with outflow obstruction. Two patients had astrocytomas, one had glioblastoma multiforme and one had lung carcinoma with metastasis to brain. LDH activities of specimens obtained by lumbar puncture were 18, 40, 57 and 20 units, respectively (Table 1). The CSF removed from the dilated ventricle in these patients had values of 29, 36, 62 and 105 units, respectively. Thus, the only elevated value was in the patient with brain metastasis from lung carcinoma.

#### Central Nervous System Infectious Diseases:

CSF LDH activity of these patients is presented in Table 2. Eight of 9 patients with meningitis, 3 with brain abscess and 3 of 8 with encephalitis had elevated LDH activity. Two with infectious polyneuritis had normal enzyme levels. There did not appear to be a direct relationship between enzyme level and cell count in patients with infectious disorders (Table 3).

#### Seizure and Degenerative Nervous Disorders:

Specimens of CSF were obtained within 3 days of seizure from 60 patients with a variety of seizure disorders. These included Grand and Petit mal epilepsy, Jacksonian, Temporal lobe, alcoholic,

febrile, postencephalitic, traumatic, arteriosclerotic and Adams-Stokes seizures. Two with grand mal epilepsy and one each with temporal lobe, febrile and Adams-Stokes seizures had elevated CSF LDH activity no greater than 100 Units.

In 17 patients with multiple sclerosis, 5 with paralysis agitans, 4 with amyotrophic lateral sclerosis, 3 with presenile dementia and one and each with syringomyelia and Huntington's chorea there were no elevations of enzyme activity.

#### Vertebral Disorders:

Of 101 patients with herniated nucleus pulposus, spondylosis or spondylolisthesis, 3 had elevated LDH activity no greater than 78 units.

Specimens were obtained within 24 hours of spinal injury in 2 patients with traumatic cord compression. The LDH activity was elevated to 100 and 246 units, the higher occurring with associated hemorrhage from the cord or vessels of the vertebral canal.

Lymphoma and ovarian carcinoma were present in 2 patients with nerve root involvement and their CSF LDH activities were normal. Metastatic cord involvement from breast carcinoma in 2 patients and from prostatic carcinoma in another showed enzyme elevations to 90, 200 and 233 units respectively.



TABLE II  
INFECTIOUS DISEASES

| CONDITION               | NO. OF PATIENTS | M  | F | RANGE OF LDH |             | NO. OF ELEVATIONS | ELEVATIONS (PER CENT) | AVERAGE LDH ACTIVITY (UNITS) |
|-------------------------|-----------------|----|---|--------------|-------------|-------------------|-----------------------|------------------------------|
|                         |                 |    |   | HIGH (UNITS) | LOW (UNITS) |                   |                       |                              |
| Meningitis              | 9               | 5  | 4 | 1500         | 70          | 8                 | 89                    | 559.8                        |
| Brain abscess           | 3               | 1  | 2 | 529          | 82          | 3                 | 100                   | 252.6                        |
| Encephalitis            | 8               | 7  | 1 | 462          | 41          | 3                 | 38                    | 119.8                        |
| Infectious Polyneuritis | 2               | 1  | 1 | 41           | 18          | 0                 | 0                     | 29.5                         |
| Total                   | 22              | 14 | 8 | 1500         | 18          | 14                | 64                    | Mean 309.7                   |

*Cerebrovascular Disease:*

Patients with thrombosis or embolism of the middle cerebral or basilar arteries and those with intracerebral hemorrhage are treated as cerebral infarctions. All had acute infarction and none clinically appeared to have had repeat infarction following the first episode.

Initial specimens were obtained within 72 hours of infarction and the results are listed in Table 4. Sixty-one percent of the patients had elevated enzyme levels. Initial LDH activity appeared to be higher in patients who died as a result of acute infarction than in those who survived. Values of CSF LDH of 100 units or more were associated with a significantly higher immediate mortality (Table 5).

In 13 patients with infarction in whom multiple CSF specimens were obtained, there was a tendency for progressive elevation of CSF LDH activity with time. These results are presented in Table 6. The CSF LDH rose significantly at 3-8 days and still higher in 9-13 days post-infarction. Four of these

13 patients died as a result of infarction and LDH level did not necessarily correlate with survival.

CSF was obtained within 72 hours of onset of symptoms from 11 patients with subarachnoid hemorrhage and LDH activity ranged from 150-200 units. The activity for 2 patients who died was not greater than that for the 9 who survived.

Two of 13 patients with arterial insufficiency had an elevated LDH activity.

*Traumatic Disorders:*

Original CSF specimens were obtained within 48 hours of trauma from patients with cerebral concussion and contusion (Table 4). The majority of patients with contusion had elevated LDH activity while none were found with concussion. Repeat determinations were performed in 7 of 9 patients with contusion up to 14 days after trauma and these results are presented in Table 6. There was a significant elevation of activity in serial specimens after injury similar to that seen following infarction. Duration of elevated activity following contusion was not determined.

Five patients with epidural and subdural hematoma had elevated LDH activity (Range 95-1261 units).

*Miscellaneous Conditions:*

Specimens were obtained from 97 subjects with various diseases involving the C.N.S. Included were cerebral atrophy, migraine headache, labyrinthitis, diabetic and alcoholic peripheral neuropathy, combined system disease, coma from infections or barbiturates and other drugs, hepatic coma, trigeminal neuralgia, familial amblyopia, retrobulbar neuritis, dilantin toxicity, hydrocephalus, pseudotumor cerebri, hypertensive encephalopathy and syphilis. Single subjects with cerebral atrophy, hepatic coma, coma complicating pneumonia and trigeminal neuralgia had elevations of enzyme activity. The highest value was 105 units. None of these disease states was consistently associated with an elevated CSF LDH activity.

TABLE III

| CONDITION                       | CSF LDH  | CELLULAR           | DIFFERENTIAL<br>CELL COUNT<br>(PER CENT) |
|---------------------------------|----------|--------------------|------------------------------------------|
|                                 | ACTIVITY | COUNT              |                                          |
|                                 | (UNITS)  | (CELLS/<br>CU.MM.) |                                          |
| <i>Meningitis (Organism)</i>    |          |                    |                                          |
| Hemophilus (Type A)             | 388      | 9,600              | 100 neutrophils                          |
| Hemophilus (Type B)             | 732      | 15,000             | "                                        |
| "                               | "        | 556                | 16,000                                   |
| "                               | "        | 1500               | 5,500                                    |
| "                               | "        | 70                 | 6,500                                    |
|                                 |          |                    | 50 mononuclear<br>cells                  |
| Pneumococcus                    | 568      | 19,000             | 100 neutrophils                          |
| Staphylococcus Aureus           | 755      | 88                 | "                                        |
| Meningococcus                   | 270      | 800                | "                                        |
| Sterile culture                 | 199      | 240                | 10 mononuclear<br>cells                  |
| <i>Brain Abscess (Organism)</i> |          |                    |                                          |
| Staphylococcus Aureus           | 529      | 60                 | 100 neutrophils                          |
| Pneumococcus                    | 147      | 7                  | "                                        |
| Sterile culture                 | 82       | 1                  |                                          |

TABLE IV  
CEREBROVASCULAR DISEASE

| CONDITION*                           | NO. OF PATIENTS | M  | F  | RANGE OF LDH |             | NO. OF ELEVATIONS | ELEVATIONS (PER CENT) | AVERAGE LDH ACTIVITY (UNITS) |
|--------------------------------------|-----------------|----|----|--------------|-------------|-------------------|-----------------------|------------------------------|
|                                      |                 |    |    | HIGH (UNITS) | LOW (UNITS) |                   |                       |                              |
| Thrombosis of middle cerebral artery | 45              | 27 | 18 | 362          | 12          | 23                | 51                    | 88.1                         |
| Embolism to middle cerebral artery   | 3               | 1  | 2  | 920          | 78          | 3                 | 100                   | 413.3                        |
| Thrombosis of basilar artery         | 6               | 5  | 1  | 196          | 22          | 4                 | 67                    | 99.0                         |
| Embolism to basilar artery           | 1               | 1  | 0  | 302          | —           | 1                 | 100                   | 302.                         |
| Intracerebral hemorrhage             | 7               | 3  | 4  | 460          | 86          | 7                 | 100                   | 242.8                        |
|                                      | 62              | 37 | 25 | 920          | 12          | 38                | 61                    | Mean 137.4                   |
| TRAUMATIC DISORDERS                  |                 |    |    |              |             |                   |                       |                              |
| Cerebral concussion                  | 5               | 2  | 3  | 74           | 16          | 0                 | 0                     | Mean 45.0                    |
| Cerebral contusion                   | 9               | 7  | 2  | 178          | 39          | 7                 | 78                    | Mean 111.6                   |

\* Initial observation in each patient.

### Discussion

Comparison of the reported studies of CSF LDH activity is difficult because different buffer systems, temperature control, direction of the reaction pyruvate to lactate and the means of expressing results were employed. Probably the only way to compare results is to consider the number of elevations associated with various disorders disregarding individual values reported.

Although interesting, the increase in LDH activity with increasing age does not appear to have a clinical application. Correction of male values for age did not produce the marked changes noted previously.<sup>9</sup>

Elevated CSF LDH activity has been found in association with cerebrovascular disease including cerebral infarction,<sup>2,3,9,10</sup> central nervous system infection,<sup>3-8,10</sup> intracranial neoplasm,<sup>2-11</sup> cranial trauma<sup>1,3,9,10</sup> and cerebral air study.<sup>2,10</sup> Several mechanisms have been offered to explain these elevations.

Elevation following cerebral infarction has been attributed to loss of LDH from the infarcted brain, proportional to the area infarcted, and to degradation of extravasated blood. It has been reported that in the absence of further infarction maximum enzyme levels were reached within 24 to 72 hours after infarction and these returned to normal in 5 to 10 days.<sup>6</sup> Release of LDH from infarcted brain or extravasated blood probably does explain a major part of the initial elevation found in some patients with infarction.

Size of infarction can only be estimated in surviving patients and no report comparing the size of infarction at autopsy with CSF LDH activity has appeared, so that no clearcut relation of size of infarct to enzyme level was demonstrated. In the

present study maximum levels were not necessarily reached in 24 to 72 hours, nor did they return to normal within 5 to 10 days (Table 6) even though there was no clinically apparent repeated infarction.

Why progressive elevations of enzyme activity should occur is not clear. Delayed necrosis could possibly explain this finding but is a less acceptable explanation in patients clinically improving from cerebral infarction.

Elevation of CSF LDH associated with subarachnoid hemorrhage has been ascribed to release of LDH by extravasated blood and that associated with meningitis to a compromise of the "blood-brain barrier".<sup>4-6</sup> In meningitis, leukocyte count does not parallel LDH activity level,<sup>5</sup> (Table 3). Leakage of plasma protein and LDH has been suggested as the cause of enzyme elevation<sup>5</sup> but this has been disputed.<sup>16</sup>

Tumor size, rate of growth and necrosis of surrounding brain tissue have been proposed as explanations of the elevated LDH levels found with cerebral neoplasm.<sup>6</sup> In early studies elevated activity

TABLE V  
CEREBRAL INFARCTION\*  
Comparison of LDH Activities in Patients Who Survived or Died

| LDH ACTIVITY (UNITS) | TOTAL CASES | SURVIVED | DIED | PER CENT OF DEATH |
|----------------------|-------------|----------|------|-------------------|
| >100                 | 21          | 8        | 13   | 61.9*             |
| <100                 | 41          | 38       | 3    | 7.3               |

\* 62 patients listed in Table IV.

\* Difference between per cent of death with LDH level < 100 or > 100 units.  $p < .001$ .



TABLE VI  
CSF LDH ACTIVITY AS A FUNCTION OF TIME  
Cerebral Infarction

| PERIOD AFTER<br>INFARCTION | NO. OF<br>PATIENTS | MEAN LDH<br>ACTIVITY<br>(UNITS) | RANGE  | NO. OF<br>ELEVATIONS |
|----------------------------|--------------------|---------------------------------|--------|----------------------|
| Day 1-2*                   | 13                 | 54.9                            | 26-118 | 2                    |
| Day 3-8                    | 13                 | 101.5†                          | 60-272 | 11                   |
| Day 9-13                   | 6                  | 242.3‡                          | 71-980 | 4                    |

Cerebral Contusion

| PERIOD AFTER<br>TRAUMA | NO. OF<br>PATIENTS | MEAN LDH<br>ACTIVITY<br>(UNITS) | RANGE  | NO. OF<br>ELEVATIONS |
|------------------------|--------------------|---------------------------------|--------|----------------------|
| Day 1-2*               | 7                  | 88.7                            | 18-210 | 5                    |
| Day 3-6                | 7                  | 180.0                           | 90-660 | 7                    |

\* Day 1 was the day of infarction or trauma.

† Difference between LDH level for day 1-2 and 3-8.

p < .01.

‡ Difference between LDH level for day 3-8 and 9-13.

.05 > p > .01.

|| Difference between LDH level for day 1-2 and 3-6.

p < .01.

was found with metastatic but not primary cerebral neoplasms<sup>4,5</sup> suggesting that grade of malignancy was responsible for the level encountered. More recent reports have not demonstrated this difference<sup>2,7,9,10</sup> nor was it seen here (Table 1).

It has been suggested that if a tumor is extradural or if it obstructs flow of spinal fluid, LDH may not reach the main stream of CSF from the tumor.<sup>6-8</sup> If meningiomas arise from arachnoid cells at or near an arachnoid villus,<sup>17</sup> it seems possible that the tumor LDH could enter the CSF. This would seem to explain enzyme elevations that have been found associated with meningiomas.<sup>2,3,8</sup> In one instance there was a high ventricular fluid LDH (105 units) and a normal CSF level (20 units) indicating that obstruction may prevent dispersion of the enzyme. Normal ventricular and spinal fluid levels in others seem to exclude obstruction as the sole explanation of the normal spinal fluid activities found with cerebral neoplasms.

The cause for initial elevation of LDH activity in cerebral contusion is probably the same as that in cerebral infarction. Progressive elevations in this condition as in infarction would suggest the operation of another factor. LDH released from extravasated blood would appear to explain the elevation in patients with epidural and initially in those with subdural hematomas. Unexplained are continued enzyme elevation in chronic subdural hematomas.

Elevations of CSF LDH activity following cerebral air studies have been attributed to the destruction of meningeal, ependymal or parenchymal cells or to irritation of these cells with liberation of LDH.<sup>2</sup>

It seems that the response of normal or altered but viable tissue to the non-specific irritation of infarction, neoplasm, infection or other stimuli should be considered as a reasonable explanation for otherwise inexplicable elevations.

CSF LDH determinations are not helpful in the differential diagnosis of CNS disease. Furthermore, normal levels are frequent in many serious disorders. On the other hand, elevations are rarely seen in normal persons so that a high level may help in the early diagnosis of obscure conditions and may help differentiate functional and organic disorders. Another use is in the prognosis of cerebral infarcts, levels of over 100 units early in the course indicating a poor outlook and levels below 100 a much better chance of survival.

### Summary

CSF LDH activity was measured in a number of normal patients and those with a variety of neurologic disorders. A significant increase in activity with increasing age was found in normal males but this did not appear to have a clinical application. Elevated CSF LDH levels help to indicate the presence of organic CNS disease. Cerebrovascular disorders are associated with elevation of CSF LDH activity more frequently than CNS neoplasms. Mechanisms postulated to explain the elevated levels in certain neurologic disorders have been discussed and tissue response to an irritative stimulus has been proposed as a basic explanation. Enzyme determinations are not necessary to establish the diagnosis in most infectious or traumatic disorders of the central nervous system or cerebrovascular disorders. Determination of LDH activity does not appear to be a conclusive method to diagnose intracranial neoplasms, degenerative disorders or those cerebrovascular disorders that could present a diagnostic problem. The overlap with normal values limits its use for prognosis in cerebral infarction.

### Acknowledgment

Acknowledgment is due the house staff physicians who helped obtain specimens, Dr. Philip Lipton for permission to include patients at Newington Veterans Administration Hospital, and Dr. George N. Bowers, Jr. of the Clinical Chemistry Laboratory, Pathology Department, Hartford Hospital, for his assistance throughout the study.

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### PARACELSUS AND HIS CRITICS

Now they say when I come to a patient, I know not immediately what ails him, but I need time to find out. It is true. That they judge immediately is the fault of foolishness; for in the end the first judgment is false and from day to day they know the longer, the less, what it is, and make liars of themselves. Whereas I desire to approach from day to day, the longer, the closer to the truth. For with hidden diseases it is not as with the recognizing of colors: in colors one sees well what is black, green, blue, etc. But if there were a curtain before it, thou also wouldst not know. To see through a curtain requires effort where there has been none before. What the eyes see can well be judged hurriedly, but what is hidden from the eyes it is in vain to conceive as though it were visible.—*Four Treatises of Theophrastus von Hohen Neim Called Paracelsus*, H. E. Sigerist (trans.-ed.), Baltimore: Johns Hopkins Press, 1941, p. 31.



# A Medical Society For The Massachusetts, York And Connecticut Physicians 1779-1790

Byron Stookey, A.M., M.D., Sc.D. (h.c.)

■ In Connecticut, as elsewhere, in the early days of this country, intercourse among communities was difficult and the sharing of knowledge and skills by physicians was accordingly restricted. The development of the early medical societies presents a picture of noteworthy purpose and determination on the part of their founders, and their survival over any number of years bespeaks the dedication of their members. Walter Steiner,<sup>1</sup> in his excellent paper appropriately read before the Litchfield County Medical Association in April 1936, gives an able description of the second medical society in Connecticut to carry on its functions for a period of years, documenting four of its meetings, 1779, 1780, 1784 and 1790. During research for his article on the first medical society in the state for which we have any record of continuing activity—the Medical Corporation in Litchfield which held its first meeting in January 1767—the author<sup>2</sup> found evidence of additional meetings of the late society reported by Steiner which seems worth recording since it establishes even greater importance for that society than has previously been recognized.

The first meeting of this society was held in Sharon July 5, 1779, in the beautiful, Georgian stone house of Dr. Simeon Smith. The report of this meeting in the Connecticut Courant was headed:

“At a Meeting of a number of Physicians from the Massachusetts, York and Connecticut States, unanimously came into the following Resolves.” The full text of their purposes, as well as the thirteen resolutions adopted, have been reproduced in Steiner’s article and consequently are not given here. It has been of interest to note that this meeting, unlike all that followed, was not preceded by one or two announcements in the Connecticut Courant, nor has the author been able to find in any other source, a preliminary notice. Possibly word of the meeting passed in person among the physicians of the towns near Sharon, Lakeville,

Kent and Canaan in Connecticut; Amenia, New York only five miles away, and Sheffield and Ashley Falls in Massachusetts relatively near.

The first of thirteen articles adopted by the society, after a lengthy preamble of two paragraphs, as given in the Connecticut Courant, states: “1st That this meeting shall be known and called by the name of the Medical Society of Sharon.”, which would seem most appropriate. The remaining twelve articles, over the signature of Oliver Fuller as clerk, are in essence similar to the eight articles adopted by the Medical Corporation in Litchfield in 1767. There is no evidence that any paper was read at the first Sharon meeting, July 5, 1779, or at the subsequent one on the last Tuesday of September. Following the organization meeting of the Litchfield Corporation, in 1767 however, Seth Bird of Litchfield gave a medical paper and Oliver Fuller an oration on the duties of the physician, both of which were the first presentations of their kind before a Connecticut medical society of which we have any record.

The description of the first Sharon meeting, 1779, contains the following:

“N.B. Any gentlemen of the faculty, that are disposed to join this medical society will meet with a kind reception, on the last Tuesday of September next, or on any of our future meetings.”

This open and generous invitation did not escape the attention of Dr. James Potter of New Fairfield. In the Connecticut Courant, October 26, 1779, appeared an announcement, essentially the same as the article concerning the original Sharon meeting, containing the same thirteen articles, except for a noteworthy difference in the *first*, which now read: “1st That this meeting shall be known and called by the name of First Medical Society in the Thirteen United States of America since their independence.” This announcement, unlike the first

*\*I should like to express my great indebtedness to the staffs of the New York Academy of Medicine, the Yale University Library, the Litchfield Historical Society and the New York Public Library.*

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and the subsequent ones which carried only the name of Oliver Fuller as clerk, was signed

James Potter, Chairman

A true copy

Test. Oliver Fuller, Clerk

and, contrary to the previous announcement, no invitation to other physicians was appended.

In the Connecticut Courant of February 15, 1780 we find:

"Notice is hereby given to the members of the First Medical Society in the Thirteen United States of America since their independence to meet at Sharon on Tuesday, the 29th day of February, next, 12 o'clock on said day.

Oliver Fuller, Secretary's Clerk."

At this meeting, also held in Dr. Simeon Smith's house, James Potter delivered his "famous" oration, which was privately printed:

An  
ORATION  
on the RISE and PROGRESS of  
PHYSIC IN AMERICA  
Pronounced before the  
FIRST MEDICAL SOCIETY  
in the  
THIRTEEN UNITED STATES  
of  
AMERICA  
since their  
INDEPENDENCE

At their CONVENTION held at SHARON, on the last day of February 1780 Together with a Word of Advice to a Candidate  
*"Will no superior Genius snatch the Quill, and save me, on the Brink, from writing ill."*

Young

Of this oration Bronson<sup>3</sup> stated "... for elaborate bombast it excels anything I have ever seen in print." and Russell<sup>4</sup> said of it, "This is the most grandiloquent of performances, abounding in high sounding, bombastic words, and lengthy sentences. . . ." Steiner fully agreed with these opinions, and the oration must have been painful to some members of the audience, at least to Simeon Smith who had studied medicine at Edinburgh and enjoyed the broadening influence this entailed, and to Oliver Fuller who was a graduate of Yale, Class of 1762. Potter was apparently hard put to it for a suitable quotation, for the one he used had appeared in an article in the Connecticut Courant of January 15, 1770 which, because of its style and lengthy sentences was, doubtless, written by Potter. In addition to his oration Potter delivered a discourse on the duties of a physician and advice to a candidate, subjects which at a meeting of the earlier

society in 1767 were presented by a member other than the one who gave the oration.

The notice of the 1781 meeting was published in the Connecticut Courant, June 15, 1781, as follows:

"This may notify the members of the First Medical Society in the Thirteen United States of America since their Independence, to meet at the Dwelling house of Dr. John Chamberlain, Amenia Precinct, Dutchess County and State of New York, on the Third Tuesday of July 1781, at Ten o'clock A.M.

Oliver Fuller, Clerk"

June 4, 1781

The next meeting was announced in the Connecticut Courant, Tuesday, May 29, 1782:

"This is to Notify the Members of the First Medical Society in the Thirteen United States of America since their Independence that a Meeting is to be attended on the second Tuesday of June next, at the house of Dr. Jonathan Chamberlain, in Amenia Precinct, State of New York, at ten o'Clock A.M.

Oliver Fuller, Clerk"

And again, another meeting was called, the notice appearing in the Connecticut Courant on May 27, 1783

"These are to notify the Members of the First Medical Society in the Thirteen United States since their Independence that a meeting will be holden at Dr. Phineas Smith's\* in Sharon, on the second Tuesday of June next, at ten o'Clock A.M.

Oliver Fuller, Clerk"

Kent, May 3, 1783

The last notice to appear in the Connecticut Courant came out in the issues of both May 18th and May 25th, 1784, reading:

"This may notify the Members of the First Medical Society in the Thirteen United States of America, since their Independence that a meeting will be attended on the last Tuesday of June next, at 10 o'Clock A.M. at the house of Dr. Oliver Fuller, in Kent.

Oliver Fuller, Clerk"

Kent, April 19, 1784

A deciding turn of events for Connecticut medicine occurred when the Medical Society of New Haven County, under the guidance of its incorporators, Leverett Hubbard, Eneas Munson, Samuel Nesbitt, Levi Ives and Samuel Darling,

\* Dr. Simeon Smith took care of two sons of his eldest brother, Phineas and Apollo, and presumably the former studied medicine under his uncle.



advertised in the Connecticut Journal, December 10, 1783 and the two succeeding issues calling a meeting of the physicians and surgeons of New Haven County for January 5, 1784, and, among other recommendations, determined, “. . . to unite with the several medical societies within the state in a joint application to the Legislature to obtain a charter.” Accordingly a circular letter was sent “. . . to the several counties, asking the appointment of delegates to meet in Hartford.” In accordance with this invitation the following announcement appeared in the Connecticut Courant April 20th and April 27th, 1784:

“Having received a letter from the Committee of Medical Correspondence appointed by the faculty of New Haven County addressed to the Physicians and Surgeons of the County of Litchfield, proposing a meeting by deposition from each county in the state at Mr. Butler’s tavern, in Hartford on the 16th day of May next, authorized to agree on an organization of the constitution of a medical society, and write in a petition to the legislature for an act of incorporation. Happy in the opportunity of seconding their generous public spirited attempt we desire a meeting of the Physicians in the County of Litchfield at David Buci’s tavern in Litchfield on the second Tuesday of May next, for the purpose above-proposed.

Seth Bird  
Lemuel Hopkins  
Daniel Sheldon

April 1, 1784”

Two of the signers of this call for a meeting, Seth Bird and Lemuel Hopkins, were the foremost physicians in Litchfield County. The former, as has been said, read the first recorded paper before a medical society in Connecticut at the meeting in Litchfield in 1767. He had studied under Dr. James Hurlbut and was one of the physicians chosen by Connecticut, in 1775, to examine physicians offering to serve in the Continental army as surgeons or surgeons’ mates.

Lemuel Hopkins studied under both Dr. Jared Potter and Dr. Seth Bird—the latter he held to be the most outstanding physician he ever knew, a view shared by many of his colleagues. Hopkins began the practice of medicine in Litchfield, later moving to Hartford where he was highly regarded as a physician. Yale College<sup>5</sup> conferred a Master of Arts degree on him in 1784. As a further honor, a medical society formed in Hartford some years after his death was named The Hopkins Medical Association.

Dr. Daniel Sheldon, who was Dr. Hopkins’ brother-in-law, practiced first in Washington, Con-

necticut and subsequently moved to Litchfield where he remained until his death.

A second meeting was called for August 2, 1784 in Litchfield “. . . to report the result of the doings of a Committee (appointed by the Physicians and Surgeons who met at Hartford last May) . . . and other matters of importance are to be attended to, it is expected there will be a general meeting.” No indication has been found that the members of the First Medical Society in the Thirteen United States since their Independence responded officially to the call of the Medical Society of New Haven County, or that they took cognizance of the action of the New Haven society in any of their succeeding announcements. James Potter, however, appeared at the second meeting of the New Haven society, February 2, 1784, and doubtless at others since “no one flitted about the state” to various societies as often as he did. Since delegates were requested from the various societies it is fair to assume that both the president, James Potter, and the clerk, Oliver Fuller, would have attended, instead only Potter appeared and Fuller was not present—a fact which may have led to his resignation as clerk. Curiously, no report of the New Haven meeting appears in any of the subsequent announcements of the 1779 society.

The following notice was published in the Weekly Monitor of February 1 and February 15, 1785:

“These may notify the Members of the first Medical Society in the Thirteen United States of America, since their Independence, that a meeting will be holden at the House of Capt. Abraham Fuller, in Kent, on the last Tuesday in June next, at ten o’Clock, A.M.

Per Order

Oliver Fuller, Secretary

Kent, Jan. 22, ’85

N.B. Inoculation will take place in Kent, in April next. All necessary Accommodations for those who have a mind to apply.

O.F.”

This is the last time that Oliver Fuller’s name appears as an officer of the society which he served as faithful clerk from 1779 to 1785. He was the son of Thomas Fuller, Jr.,<sup>6</sup> and grandson of Thomas Fuller, both of East Haddam, Connecticut. On May 3, 1767 he married Alice Ransom of Colchester, who died October 1, 1776, and a year after her death he married Lois Gillett. One son, Thomas, by his first wife, became a physician in New York. Fuller, who was made a member of the Connecticut Medical Society in May 1793, lived and practiced in Kent where he died on March 9, 1817 at the age of seventy-five.

"Dr. Josephine Evarts has been kind enough to inform me that Oliver Fuller is buried in Good Hill Cemetery in Kent, beside his first wife. His tombstone bears the following inscription:

Doctr. Oliver Fuller  
died March 9, 1817  
aet 75"

The notice for the 1786 meeting also appeared in the *Weekly Monitor*, in the editions of May 23 and 30, as follows:

"The first Medical Society etc. meet at Doctor Phineas Smith's in Sharon on the third Tuesday of June next.

Samuel Rockwell, Sec'ry  
Sharon, May 4, 1786"

No notice of a meeting in 1787 appeared in either the *Connecticut Courant* or the *Weekly Monitor*, but in the latter journal of June 2, 9 and 16, 1788 we find the following:

"The annual meeting of the United Medical Society will be holden at *Gallow's Tavern* in Sharon, on the third Tuesday of June next, at ten o'clock A.M. of which all concerned are desired to take notice.

Samuel Rockwell, Sec'ry  
Sharon, May 14th"

A similar notice appeared for a meeting in Sharon in June 1789 at the house of Mr. Joseph Gallow, the society being again called the United Medical Society. The last meeting of which there is any record took place on the third Tuesday of June, 1790 in New-Fairfield, the home town of Dr. James Potter. The announcement of this meeting appeared unsigned in three issues of the *Weekly Monitor* as follows:

"The Members of the U.S. *Medical Society*, are reminded, that their Annual Meeting will be holden at New-Fairfield at the House of Mr. John Hubbel on the third Tuesday of June next at 10 o'clock A.M.  
May 24, 1790"

The incorporators of the Medical Society of New Haven County and its members had striven ardously to obtain a state charter and to indicate

to the legislature that their efforts represented the hopes and desires of the profession throughout Connecticut. They urged physicians to form societies in each county and invited some from other sections to join the New Haven Society. Accordingly, in 1791, James Potter,\* among others, was elected to their membership. The eight year struggle of the members of the Medical Society of New Haven County to obtain a state charter gained the interest and support of the physicians of Connecticut for which we have any record of continuing activity—the society which began in the north-western reaches of the state in 1779 as the Sharon Medical Society for the "Physicians from the Massachusetts, York, and Connecticut states"—came to an end after eleven years of service to the profession.

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\* Curiously, James Potter's home county, Fairfield, was, according to Rufus Blakeman,<sup>7</sup> not organized until a few months subsequent to the incorporation of the state society by the legislature in May 17, 1792. In spite of the efforts of the New Haven Society over the years prior to Potter's election in 1791 it seems strange that his name "... stands at the head of corporators, forty-six in number, six of whom were from New Haven County."

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*Man is not the creature of circumstances. Circumstances are the creatures of men.*

—Disraeli



174th ANNUAL MEETING  
of the  
CONNECTICUT STATE MEDICAL SOCIETY

Statler-Hilton Hotel  
10 Ford Street, Hartford, Connecticut  
April 26, 27, 28, 1966

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PROGRAM COMMITTEE

PAUL F. McALENNEY, *New Haven, Chairman*

RUDOLF E. KLARE, *Woodstock*

DAVID BABBOTT, *Hartford*

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PRELIMINARY PROGRAM

Tuesday April 26

MEZZANINE FLOOR

ANNUAL MEETING OF THE HOUSE OF DELEGATES

KENNETH F. BRANDON, *Hartford, Speaker of the House, presiding*

10:00 CALL TO ORDER  
BUSINESS SESSION

1:00 LUNCHEON FOR OFFICERS, MEMBERS OF THE HOUSE AND GUESTS

2:00 RESUMPTION OF BUSINESS

## Wednesday, April 27

9:00 REGISTRATION—MEZZANINE

TERRACE ROOM

9:30 CALL TO ORDER—President of the Society

ADDRESS OF WELCOME—President, Hartford County Medical Association

9:45 DRUG INDUCED HEPATIC INJURY

FENTON SCHAFFNER, New York, New York

10:30 HEPATIC DISEASE—SOME RECENT ADVANCES IN TREATMENT

WILLIAM H. J. SUMMERSKILL, Rochester, Minnesota

11:10 INTERMISSION TO VISIT TECHNICAL EXHIBITS

11:40 POLYCYTHEMIA

LOUIS R. WASSERMAN, New York, New York

12:20 POST TRAUMATIC EPILEPSY

A. EARL WALKER, Baltimore, Maryland

1:00 LUNCHEON—CITY ROOMS

INTERMISSION TO VISIT TECHNICAL EXHIBITS

2:00 DISORDERS OF CORTISOL PRODUCTION

FRANK H. TYLER, Salt Lake City, Utah

2:40 THE BATTERED CHILD WITH INNOCENT PARENTS

JOHN CAFFEY, Pittsburgh, Pennsylvania

3:30 **Meetings of Sections of the Society and Guest Organizations**

Section on Dermatology

Section on Gastroenterology }  
Section on Internal Medicine } Joint Meeting

Section on Neurology }  
Section on Neurosurgery } Joint Meeting

Section on Obstetrics and Gynecology

Connecticut Society of Pathologists

Section on Pediatrics (Hezekiah Beardsley Club)

Section on Physical Medicine

Section on Preventive Medicine and Public Health

Section on Proctology

Section on Urology

Connecticut Diabetes Association

7:00 **Annual Dinner of the Society—Terrace Room**

Guest Speaker: DURWARD G. HALL, M.D.  
Congressman from Missouri



## Thursday, April 28

9:00 REGISTRATION—MEZZANINE

### TERRACE ROOM

9:45 ORGAN TRANSPLANTS—MEDICAL MANAGEMENT

EDWARD B. HAGER, Boston, Massachusetts

10:30 ORGAN TRANSPLANTS—SURGICAL MANAGEMENT

RICHARD E. WILSON, Boston, Massachusetts

11:10 INTERMISSION TO VISIT TECHNICAL EXHIBITS

11:40 THE USE OF DIURETICS

WILLIAM B. SCHWARTZ, Boston, Massachusetts

12:20 OFFICIAL INVESTIGATION OF SUDDEN SUSPICIOUS AND VIOLENT DEATH—WHAT IS NEEDED

MILTON HELPERN, New York, New York

(Program arranged with Association of Medical Examiners of Connecticut)

1:00 LUNCHEON—CITY ROOMS

INTERMISSION TO VISIT TECHNICAL EXHIBITS

### **Program Arranged with the Connecticut Society of American Board Surgeons and the Section on Orthopedics**

2:00-3:30 A SYMPOSIUM ON TRAUMA

Moderator: WILLIAM W. L. GLENN, New Haven

Panel: RONALD A. MALT, Boston, Massachusetts

FIORINDO A. SIMEONE, Cleveland, Ohio

JOHN D. STATES, Rochester, New York

3:30 **Meetings of Sections of the Society and Guest Organizations**

Section on Allergy

Section on Anesthesia

Section on General Practice

Section on Ophthalmology

Section on Orthopedics

Connecticut Society of American Board Surgeons

} Joint Meeting

Section on Otorhinolaryngology

Connecticut District Branch—American Psychiatric Association

Section on Radiology

Association of Medical Examiners of Connecticut

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include: skin rash, nonthrombocytopenic purpura with petechiae, ecchymoses, peripheral edema, fever and transient leukopenia; also, very rarely, fainting spells, angioneurotic edema, bronchial spasm, hypotensive crisis, anuria, stomatitis, proctitis and anaphylaxis. Other serious effects have occurred after concomitant administration of meprobamate and other drugs. Massive overdosage may produce grave effects.

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Josephine P. Lindquist  
*Assistant to General Manager*

## SUMMARY OF ACTIONS COUNCIL MEETING

Wednesday, January 26, 1966

### I. Attendance

Present in addition to the Chairman, Dr. S. J. Martin, were: Drs. Cullen, Hess, Bradley, Goldberg, W. Martin, Weise, Sr., M. Caplan, Brandon, Rogol, Grendon, Egan, Spitz, Palumbo, Shepard, Nolan, Ciccarella, Cramer, Abbot, Petrie, Wilson, Hastings, and Roch. Also present were: Mrs. Lindquist, Mr. Chilcoat (AMA) and Dr. Richards. Absent were: Drs. Gardner, H. Caplan, Pitock, Ayres, Fabro and Epstein.

Invited guests attending the meeting were: Dr. Hyman A. Levin, New Haven, and Dr. Franklin M. Foote, Commissioner of Health.

### II. Routine Business

#### Approval Of Minutes

As printed and distributed, it was VOTED to approve the minutes of the meeting of December 9, 1965.

#### Life Membership

It was VOTED to approve applications for Life Membership of the following eligible Active Members of the Society:

I. L. Amos, Danbury (FCMA)  
Walter Blogoslawski, Hartford (HCMA)  
Waldo F. Desmond, Newtown (FCMA)  
K. Gregory Elliot, W. Hartford (HCMA)  
David L. Ellrich, Westport (FCMA)  
Mark A. Gildea, Bridgeport (FCMA)  
Nicholas A. Giorgio, W. Hartford (HCMA)  
Harry Golston, Hartford (HCMA)  
I. L. Harshbarger, Bridgeport (FCMA)  
Harold A. Howard, Wethersfield (HCMA)  
Dewey Katz, Hartford (HCMA)  
Samuel Marranzini, Hartford (HCMA)  
Frederick W. McFarland, Stamford (FCMA)  
Fritz M. Meyer, Bridgeport (FCMA)  
Henry J. Murray, Stamford (FCMA)  
Denis S. O'Connor, New Haven (NHCMA)  
Egmont J. Orbach, New Britain (HCMA)  
Francis Paul, Norwalk (FCMA)  
Peter Pileggi, Bridgeport (FCMA)

Irving Platt, New Haven (NHCMA)  
Thomas Preston, Hartford (HCMA)  
William H. Resnik, Stamford (FCMA)  
Peter J. Scafarello, Hartford (HCMA)  
Nathan R. Tolk, Bridgeport (FCMA)  
William H. Upson, Suffield (HCMA)  
Francis B. Woodford, Ridgefield (FCMA)

#### Election Of Student Members

It was VOTED to elect 9 Connecticut residents, who are attending schools of medicine, to Student Membership in the Society. Their names will be published in an early issue of the Journal.

#### Resignations And Appointments—Committee On Accident Prevention

It was VOTED to accept the resignations of two members of the Committee: Clement C. Clarke, New Haven, and Vincent J. Turco, Hartford. It was further VOTED to appoint Isao Hirata, Jr., New Haven, to membership on the Committee.

#### Replacement—Chairman Of Subcommittee To Study And Revise The Bylaws

By closed ballot, it was VOTED to elect J. Alfred Fabro, Torrington, as Chairman of this Subcommittee of the Council, to replace Jachin B. Davis, New Haven, who is no longer a member of the Council.

#### Confirmation—Interim Authorization Of The Chairman

It was VOTED to confirm an interim authorization of the Chairman to have Charles B. Cheney, New Haven, a member of the CSMS Committee on Medical Education and Licensure, attend the 62nd National Congress on Medical Education, Chicago, February 3-8, and to reimburse Dr. Cheney for usual expenses in the amount of \$250 (approx.). As a representative of the Society, it is understood that Dr. Cheney will file an informative report with the Council on the proceedings of the Congress.

#### Confirmation—Interim Appointments Of The Chairman

It was VOTED to confirm appointments of the Chairman to have Peter J. Scafarello, Hartford, and Isadore H. Friedberg, Newington, represent the Society at an AMA National Conference on Federal Medical Assistance Programs, Chicago, January 20-



21, at the expense of the AMA. A report on the proceedings of the Conference, filed jointly by Drs. Scafarello and Friedberg, was received too late to present at this meeting. It will be reproduced for distribution to members of the Council, the Committees on National and State Legislation, and the Committee on Third Party Payments and the Advisory Committee on Welfare, Finance and Control, and will be submitted for Council acceptance at the next meeting.

**Representative To AMA Legal Conference**

In response to a request from AMA, it was VOTED that if Max Caplan, Meriden, attended this Conference as a representative of another agency, he also serve as the representative of the Society and report to the Council on the proceedings of the Conference.

**Appointment—Committee On Medical Quackery**

In response to a request from the AMA, it was VOTED to appoint Max Caplan, Meriden, chairman of a Committee on Medical Quackery (to include chiropractic problems, if any), and to ask Dr. Caplan, in consultation with the President, to recommend for appointment by the Council other members of the Society to serve on the Committee.

**Date Of Next Meeting**

The next meeting of the Council was scheduled for Thursday, February 17, 1966.

**III. Old, New And Special Business**

**Report—AMA National Symposium On Venereal Disease**

Hyman A. Levin, New Haven, filed a written report on his attendance at this Symposium as a representative of the Society, and joined the Council to augment his report in person. Commissioner Foote of the State Health Department was also present, and participated in the discussion of Dr. Levin's report. It was VOTED to accept the report, with commendation, and to refer it to the Committee on Public Health for study and recommendations, in concert with the Health Commissioner, with a view toward committing the Society to the support of efforts of the Health Department and others to make health and sex education a meaningful, regular part of the curricula of public schools and state-supported colleges and universities.

**Presentation—Certification Of Institutional Providers Under Medicare**

Invited by the Council, Health Commissioner Franklin M. Foote joined the meeting to present and make a progress report on the work of the agency in his Department which is carrying out the

program of certification of providers of institutional-type services under Part A of P.L. 89-97. He described the immediate and continuing role the agency expects to play in such areas as standards of services, utilization review committees, etc. After a considerable period of time devoted to "questions and answers," it was VOTED to thank the Commissioner for his attendance and presentation, and to request him to repeat his visit, from time to time, as the certification program progresses. In keeping with a suggestion of Dr. Foote, it was further VOTED that, on written request, the Council act favorably to appoint a "small committee of CSMS members to advise the Commissioner and his agency on the professional aspects of certification criteria and related matters."

**Reports—The Committee On Hospitals**

Three reports were received from the Committee on Hospitals. The subject of the reports and the actions taken thereon follow:

(a) *AMA Resolution on "Physician Representation In Areawide Hospital Planning*

It was VOTED to accept as information the Committee's favorable report as to the implementation of this Resolution in Connecticut, with its attendant information concerning the Society's participation in the newly-formed Hospital Planning Commission being activated under the auspices of the Connecticut Hospital Association.

(b) *"Point-System of Rating Convalescent Hospitals and Nursing Homes:"* Enlarging on its previously submitted preliminary findings, the Committee filed a final report on this subject. In brief, it is the Committee's opinion that the point-system is more arithmetical than medical, but that, at the present time, it is probably the most practical way of evaluating extended care facilities in the State. It was VOTED to accept this report as information.

(c) *Plans for Seminar on "The Implementation of Medicare in Connecticut."* It was VOTED to accept as information a report of the Committee on its plans, in cooperation with the CHA's Council of Professional Practice, to conduct a seminar on implementing Part A of Medicare, New Haven, April 20, 1966. The audience will be made up of hospital medical staff representatives, hospital administrators and directors, representatives of CSMS sections on hospital-based specialties, fiscal intermediaries, and others who have a known interest in the subject.

**Report—Ad Hoc Committee On CSMS Staff Structure**

Acting for this Committee, Orvan W. Hess, Chairman, filed a report containing two recommendations which summarized the Committee's

final evaluation of the Society's public relations needs at the present time and for the future. It was VOTED unanimously to accept the report and recommendations, and to direct the Committee to set about implementing its recommendations without delay.

**Directives To The Council—House Of Delegates,  
December 9, 1965**

(a) *NHCMA Resolution*: It was VOTED to refer this resolution (concerned with various matters relating to payment of physicians for their services) to the Committee on Third Party Payments, supplemented by county association representatives and Council representatives appointed by the Chairman, for study and report to the Council prior to the April 26 meeting of the CSMS House of Delegates.

(b) *Resolution on Reports of Officers and Others at Semi-Annual Meetings of the CSMS House of Delegates*: It was VOTED to refer this resolution for study, report and recommendations to an Ad Hoc Committee composed of the Speaker of the House, the Vice-Speaker and the General Manager. In brief, the resolution calls for, as far as possible, publishing the reports and remarks of officers, delegates and committees in the Delegate's Handbook mailed out with the call to semi-annual meetings of the House. It was further VOTED to inform the Ad Hoc Committee that the Council favors the intent of the resolution, but feels that officers should be privileged to augment (orally) their written reports at the meetings.

(c) *COMPAC Dues Billing*: It was reported that, as directed by the House of Delegates, billings for voluntary COMPAC-AMPAC membership dues have been included on the same statement as billings for CSMS and county association membership dues. At the time of this report, the returns were insufficient to draw any conclusions as to the efficacy of this new approach to enrolling COMPAC-AMPAC members. The report was received as information.

(d) *The 1965 Kerr-Mills (MAA) Amendments*: Received as information was the report that it had not been possible to get this item on the agenda of the Special Convention of the General Assembly held on January 13, 1966. The purpose of the House in seeking to accomplish this was to give the Assembly an opportunity to correct its "legislative oversight" in amending the MAA Statutes at the 1965 session so as to deprive elderly beneficiaries of their right to have institutional care under the direction of the physicians of their choice. Reason for lack of success: Legislative Committee reported that the legislative leaders had decided to leave the

business of the Special Session to two specific items and would not permit other "meritorious" matters to be added. Under this item, Dr. Hess reported that, at the request of Dr. Cullen, he had joined representatives of the state government, insurance companies, etc. in making a television and radio tape designed to bring various facets of the Medicare Law to the attention of the public. Part of the program's purpose, he reported, was to urge the elderly to sign up for Medicare's Part B without delay, but that since so little was known about the specifics of Part B at that time, he had felt obliged to exercise caution in making any "sales-pitch" for hasty enrollment.

**Report—Committee On Investments**

It was VOTED to receive as information a current report (through 12/1/65) of the Committee on Investments, presented by Isadore S. Goldberg, Chairman (Treasurer). In brief, the report presented evidence of a modest but steady growth in the value of investments made with a portion of the Society's reserve funds.

**Second Request—Committee To Study Perinatal  
Morbidity And Mortality**

As reported in the minutes of the meeting of November 17, 1965, the Council voted to approve, "in principle," plans for holding a seminar on Perinatal Problems; to underwrite only a "nominal part" of the estimated cost of \$2,705; and to urge the Committee to seek other sources of co-sponsorship and co-financing, including commercial sources. In a second request, presented at this meeting, the Committee reported that it was unanimous in its feeling that commercial subsidy should not be sought; that commitments totalling \$1850 had been obtained from two voluntary sources; and that, in effect, the Committee was now requesting the Council to agree to underwrite the balance of the estimated cost (approximately \$800-1000).

After considerable discussion, including a review of allocations in the 1966 Budget, it was VOTED to offer the Committee the sum of \$500 as the Society's contribution to the costs of the proposed seminar; to recommend that the Committee continue to seek additional financial support from other sources; and to suggest that the Committee consider assessing a suitable "registration fee" (as the Committee on Hospitals is doing for its April Medicare Symposium) to defray the costs of the social functions of the seminar (lunches, dinners, cocktails, etc.).

**Nominations To The "Hospital Planning Commission"**

The Council was advised that five of its six nominees for service with the Hospital Planning Commission had accepted such service and been



elected to membership on the Commission, representing medical practice, as follows:

Thomas M. Feeney, Hartford  
Leopold M. Trifari, Hamden  
Waldo E. Martin, Milford  
E. Tremain Bradley, Norwalk  
Bruce R. Valentine, Abington

The sixth nominee, G. S. Gudernatch, Sharon, had declined to serve with the Commission, because of other professional commitments, and had so notified the CHA authorities. Recognizing that the Planning Commission had been formally incorporated on January 25, 1966, and that the incorporation may have changed the *modus operandi* for electing new members, the Council felt it remained important to have a full complement of six representatives of medical practice on the Commission, and therefore VOTED to direct the nominating committee, made up of the President, the Chairman of the Council and the Chairman of the Committee on Hospitals, to select a sixth nominee and submit same to the Commission.

#### **Notification From CSMS Section On Physical Medicine**

It was VOTED to accept, as information, official notice that the CSMS Section on (the Connecticut Society of) Physical Medicine has voted to adopt a resolution in favor of fee-for-service (separate billing) for all physicians, in keeping with similar positions adopted by the CSMS Sections on Radiology and Pathology.

Pursuant to this action, it was further VOTED to communicate with the officers of all these Sections, asking how the Society might assist them in furthering the intent of the resolutions adopted by the House of Delegates (December 9, 1965) concerning support of separate billing to all patients by hospital-based specialists.

#### **Report—Committee On Accident Prevention**

Reporting on a matter previously referred to it by the Council, the Committee is of the opinion that a physician examining an applicant for possible service as a school bus or other public vehicle operator may not only attest to the physical findings elicited by his examination, but may also certify the examinee as physically qualified to operate such vehicles without incriminating or legally involving himself by so doing. It was VOTED to accept the report of the Committee, and to inform the Board of Directors of HCMA (who originally requested an opinion in the matter) that the Council concurs with the opinion of the Committee.

#### **Request For Opinion—HCMA**

Having received a request from the Board of Directors of HCMA for a Council opinion on the

question of "the legality of performing voluntary vas ligations to prevent conception when it (the operation) is agreed to by a husband, a wife and a physician," it was VOTED to recommend to the HCMA Board that this matter of legality be studied locally. From the discussion engendered by this question, it appeared that some members of the Council felt the request was for an opinion as to the *medical* (ethical) legality of the procedure, and, if so, that the Council should take no position in this regard. Others appeared to feel that since policy has been established by some individual hospital medical staffs with respect to sterilization and related procedures, it might be better to "let sleeping dogs lie." In any event, a motion to reconsider the question (with a view toward obtaining formal legal opinion from the Society's attorneys) failed to receive the required two-thirds affirmative vote.

#### **The DeBakey Legislation—Heart Disease, Cancer And Stroke**

It was VOTED to receive as information an informational report on the present status of plans to implement this legislation in Connecticut, with the Yale and UConn Schools of Medicine to be the "centers" around which a "regional medical program" will be constructed. It was further VOTED to request the President to write to the Deans of the two medical schools concerning the Society's interest in the Connecticut implementation of P.L. 89-239, and offering the assistance of the Society in the preliminary planning for such implementation.

There appeared to be general agreement that it would be desirable for the Society to have available for reference and/or specific purposes sets of "policy statements," "guiding principles," "preferred objectives" or "minimum standards" on both Medicare and the DeBakey legislation, and it was therefore VOTED to request the Committee on Hospitals (which has been studying these laws) to make recommendations to the Council which might be used as the basis for developing such statements, objectives, etc., hopefully in time to be discussed at the next meeting. The latter Committee's previously submitted report on Medicare utilization review committees was advanced as an example of what is desired.

**N.B.:** *The foregoing is a summary of the proceedings and actions of the Council on January 26, 1965. Detailed minutes of the meeting are on file at 160 St. Roman Street, New Haven, for heretofore and interested members of the Society.*

#### PLACEMENT WANTED

**DERMATOLOGIST**—Broad background with extensive training. Seek group association, position or desirable practice location upon completion of residency in June, 1966. Board eligible, military obligations completed.

**GENERAL SURGEON**—Board certified, sub-specialty training in Head and Neck surgery. Especially interested in Derby-Ansonia or Danbury areas.

**INTERNIST**—Board certified, 33 years of age, military obligations completed. Would like to practice in a medium to large community with an associate or group, but will consider solo practice as well. Available immediately.

**OBS.-GYN.**—Board eligible Obs.-Gyn. with Connecticut license wishes to locate in practice in Connecticut with either a partner or group. Will consider a solo practice as well. Available immediately.

**PATHOLOGIST**—Board certified in Clinical Pathology and eligible in Anatomic Pathology and Internal Medicine. Connecticut license. Degree in Public Health. Wishes to locate in Connecticut in a situation that will allow full use of diversified training.

#### PLACEMENT OPPORTUNITIES

**WANTED**—House Physician—diversified duties in accredited, voluntary hospital. Connecticut license required, no weekends. \$15,000 yearly. Please reply to: P. O. Box 638, Bridgeport, Connecticut 06601.

**INTERNIST**—Board eligible or certified Internist with sub-speciality training in Gastroenterology to join a multi-specialty group in New Britain. Eligibility for, or Connecticut license required.

**INTERNIST**—Board certified or eligible Internist needed to take over fully established practice and office of physician who is going into Peace Corps shortly. Located in Glastonbury, Connecticut, just a few minutes from Hartford Hospital.

**ANESTHESIOLOGIST**—Board certified or eligible Anesthesiologist to serve in 65 bed, fully accredited rural hospital which serves two communities of about 40,000 total population.

G.P.'s needed for Wallingford-Meriden area for private practice in a rapidly growing, industrial area of Connecticut. For further information, contact M. J. Esposito, M.D., 335 Cook Avenue, Meriden, Connecticut.

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**CLINICAL DIRECTOR** for Medical-Surgical Service in a decentralized 2300-bed mental hospital. Active teaching program in psychiatry, affiliated with Yale University. Fully staffed medical service. Board certified or eligible Internist preferred. Salary range: \$15,460-\$20,000. Fringe Benefits: 3 weeks' paid vacation, 3 weeks' paid sick leave, 11 paid holidays, free Blue Cross, CMS and Major Medical insurance. Contact John F. Lowney, Jr., M.D., Superintendent, Connecticut Valley Hospital, Middletown, Connecticut.

**CLINICAL OPENINGS** for physician, internist or general medical background to practice in association with other physicians; merit system, attractive salary and retirement program with excellent

sick leave, vacation and insurance benefits. **WRITE:** State Health Department, 79 Elm Street—Room 301, Hartford, Connecticut 06115. **EQUAL OPPORTUNITY EMPLOYER.**

**WANTED, COLLEGE PHYSICIAN** — for women's college, 1400 students. Out-patient and in-patient services, with nursing staff and laboratory. Full-time or part-time. Write: Mary N. Hall, M.D., Connecticut College, New London, Connecticut.

### 1966 MEETINGS

**March 24** — 182nd Annual Meeting of the New Haven County Medical Association to be held at the Waverly Inn, Cheshire, Connecticut. Business Meeting tentatively set for 3:30 P.M.  
**March 30**—Second Symposium on Kidney Disease by the Kidney Foundation of Connecticut to be held at the Mary S. Harkness Auditorium, Yale University, New Haven, Connecticut. Program sessions 9:00 A.M. to 5:00 P.M. Registration Fee \$5.00.

**April 26-28** — 174th Annual Meeting of The Connecticut State Medical Society to be held at the Statler-Hilton Hotel, Hartford, Connecticut.

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should be considered cause for immediate discontinuation of DBI at least until normal blood pressure has been restored and is maintained without vasopressors. Should lactic acidosis occur from any cause, vigorous attempts should be made to correct circulatory collapse, tissue hypoxia, and pH. **Contraindications:** Severe hepatic disease, renal disease with uremia, cardiovascular collapse. Not recommended without insulin in acute complications of diabetes (metabolic acidosis, coma, severe infections, gangrene, surgery). **Pregnancy Warning:** During pregnancy, until safety is proved, use of DBI, like other oral hypoglycemic drugs, is to be avoided.

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# Letters To The Editor

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## To The Editor:

The suspension of a physician from his county medical association is a very severe punishment. When an M.D. is suspended, he can be deprived of his hospital privileges. He cannot move to another state, because the primary condition to obtain a reciprocity license is "good standing" in his original county association. He may lose a lifetime opportunity of a job, for which he is particularly qualified. Thus, the word suspension, which on the surface does not appear cruel at all, is in fact a quasi complete destruction of a colleague's career.

To deserve such a punishment an M.D. must be guilty of very serious unethical acts. A simple complaint of a third party, which is not satisfied with a doctor's bill, when the patient was pleased with the doctor's care and not only paid the bill, but also showed his appreciation in some other way, cannot and should not be used by a committee on ethics to whip and to break down a member of the medical profession. To treat a doctor this way is "to take away all liberty from one's action and thoughts." This is in flagrant contradiction with Article 1, Section 1 of "The Duties of Physicians to Each Other" (Principles of Medical Ethics, American Medical Association). Coming from a committee on ethics, which is supposed to be a watchdog over other members of the association, it is particularly distasteful.

Why the insurance companies are trying to use an ethical committee to keep doctors under their control is difficult to understand. Instead of promising to pay 100% or 80% of a doctor's bill, they could state clearly the maximum amount they would pay for each medical act. They would thus have no need to interfere in the relationship between doctor and patient.

For a committee on ethics to order a doctor to reimburse to a patient a few dollars, which he paid his doctor with gratitude, in order to please an insurance company, is to forget that the primary role of a medical association is to uphold the doctor's dignity and to protect the doctor-patient relationship.

I think, it is high time for all of us to ask ourselves the question "Quo vadis, Medicus" and after reflection, to act the right way. To begin with, we should make it a rule that "no member of a county medical association will be suspended without a vote of two thirds of the members present at a regular or special meeting of the association."

MARCEL THAU, M.D.  
Hartford, Conn.

*This letter was referred to Dr. Fabro who has the following to say about Dr. Thau's communication.*

Dr. Marcel Thau's letter raises several interesting issues, mainly by implication. Its essence seems related to the procedures in handling questions related to fees.

Regarding the questions of fact in the case of the suspension of a physician, I can of course say nothing. But as to the procedure to be used in such cases, I can make several observations resulting from my experience as chairman of the subcommittee on censorship questions of the Council.

Although Dr. Thau's motion is a valid one for consideration, we ought to examine our county bylaws to evaluate our methods for handling problems related to fees.

Especially with Medicare and major medical insurance we will note use of the expressions: "usual and customary," and "reasonable," and "prevailing" fees. Who is to determine these? Each county society should have a committee to answer requests about such fees and to give information. This committee is usually called a Review Committee. It is not disciplinary.

Complaints by third parties about fees should be handled by a different procedure. This committee is usually called a Grievance Committee. It also is not disciplinary. It acts to arbitrate and resolve complaints about fees.

Then there are fees so unconscionable as to reflect on the good name of the profession. Such fees can be grounds for disciplinary action by a county medical society if a fee charged by one of its members is so exorbitant as to represent an infraction of our principles of medical ethics.

It is quite important that a county's methods and procedures for handling fees be carefully considered. The above differences in function and procedure may seem subtle, but they are definite and important.

I would like to remind Dr. Thau that every member is protected by the right to appeal of any county action to the Council, and "... its decision in all such matters shall be final." (Article 7, section 1, paragraph 4.) Although I seriously doubt that any committee of doctors is being "used" by insurance companies, after the C.M.S. episode of several years ago, Dr. Thau is right in being alert.

One last point: Is the primary role of a medical association to uphold the doctor's dignity—as Dr. Thau states?

J. A. FABRO, M.D.  
Torrington, Conn.

*Letters to the Editor are welcome and will be published for informative and educational purposes as space permits. As with other material which is submitted for publication, all letters will be subject to the usual editing. Address all correspondence to: THE EDITOR, CONNECTICUT MEDICINE, 160 St. Ronan Street, New Haven, Connecticut, 06511.*

## THE CONNECTICUT PHYSICIANS' ART ASSOCIATION 1966 EXHIBITION

The Connecticut Physicians' Art Association is planning the 1966 art exhibit in conjunction with the annual meeting of The Connecticut State Medical Society. This will be held at the Statler Hilton, Hartford, Conn. on April 26, 27, 28, 1966.

All previous exhibitors are invited to show their works at this meeting and new exhibitors among physicians and their families are cordially invited to join the group of art hobbyists. Works eligible will include oil, water color, tempora, black and white, etchings, photography, pastels, sculpture and ceramics. Eligible exhibitors are members of The Connecticut State Medical Society, their wives, and children. Art works will be judged in four categories: 1. children through 16 years (over 16 will be judged with adults); 2. beginners to three years; 3. over three years; 4. professional.

*Fee:* A hanging fee of one dollar (\$1.00) will be charged for each entry and fifty cents (\$.50) for children under 16 with three pictures allowed per artist.

Pictures should be framed and wired for hanging. The exhibition will be judged by professional artists.

A special effort will be made to recognize merit in each group so it is important to fill in the entry blank completely stating the number of years that you have been enjoying this hobby. Professional artists are welcome and will be judged in the professional class.

Art works must be submitted to a representative of the Art Association in the lobby of the Statler Hilton Hotel on Sunday, April 24th between the hours of 12 and 3 P.M. Parking temporarily near the side entrance is possible for the few minutes involved in dropping off these art works. Please forward entry blanks and checks to the address listed below *prior* to April 15th. Make checks payable to: *Connecticut Physicians' Art Association*.

Members who wish to exhibit may contact the following chairmen for further information and additional entry blanks:

Stewart J. Petrie, M.D., 56 Minerva Street, Derby, Conn., president, Connecticut Physicians' Art Association.

Mrs. Orvan Hess, 29 Old Orchard Road, North Haven, Conn., vice president.

Edward Williams, M.D., 269 Church Street, Naugatuck, Conn.

Charles O'Neil, M.D., 18 Asylum Street, Hartford, Conn.

Herman Austrian, M.D., 935 White Plains Road, Trumbull, Conn.

Other auxiliary members that may be contacted if further information is needed include:

Mrs. Ernest Rosenthal, 17 Pine Street, West Hartford ..... Hartford County

Mrs. Merrill Rubenow, 68 Butternut Road, Manchester ..... Hartford County

Mrs. David Waskowicz, 35 Whitemen Road, New Britain ..... Hartford County

Mrs. Clarence Harwood, 1350 Old Mill Road, Middletown ..... Middlesex County

Mrs. Ralph Gilman, Willow Brook Road, Storrs ..... Windham County

Mrs. William S. Maurer, Babcock Hill Road, South Windham ..... Windham County

Mrs. Mark Hayes, 163 Ridgewood Avenue, North Haven ..... New Haven County

Dr. Stephen Magyar, 375 George Street, New Haven ..... New Haven County

Mrs. Albert Gosselin, RFD No. 4, Norwich ..... New London County

Mrs. Roland A. Mariani, 99 Ocean Avenue, New London ..... New London County

Since a good art show will add much to the success of this meeting, participation and cooperation of all art hobbyists is solicited.

STEWART J. PETRIE, *President*,  
Connecticut Physicians' Art  
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56 Minerva Street,  
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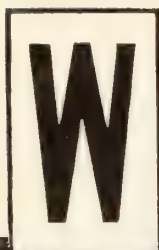
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## AROUND THE STATE

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### **New Haven County**

The 182nd Annual Meeting of the New Haven County Medical Association will be held at Waverly Inn, Cheshire, on Thursday, March 24th at 3:30 P.M. This is the first meeting since the change in By-Laws which will make attendance at a meeting once in two years a requirement for membership. It is at the annual meeting that the ladies are our guests. The agenda is made up with this in view.

The Woman's Auxiliary will be entertained in the afternoon by Mr. Frederick Sternberg of "Flowerland" with an illustrated talk on "Flower Arrangement."

The agenda for the county members will call for the election of officers, committee members and alternate delegates for the year 1966-67, and those provisory members recommended by the Committee on Credentials and Orientation.

A social hour and dinner will follow at which time Dr. Luca Celentano will be presented with the Retiring President Placque.

To make the evening program memorable, Dr. Charles Verstandig's committee has arranged an entertainment program by Shearen Elebash of Montgomery, Alabama. Mr. Elebash is an exceptional pianist and entertainer, combining a program of wit with concert artistry. His performance will make this an evening to be remembered, along with others of the past which we still talk about.

H. A. LEVIN, M.D.  
*Clerk*

### **Board Of Governors New Haven County Medical Association January 27, 1966**

The first meeting of the Board of Governors of the New Haven County Medical Association in the year 1966 was held on Thursday, January 27, 1966 at the Colonial House, Hamden, with Dr. Luca Celentano, presiding.

None of these meetings are simple routine. Of interest, I mention that plans were discussed for the Annual Meeting to be held at Waverly Inn, on March 24th. The Ladies Auxiliary will be guests of the Association. Since this will also be the first of our meetings at which attendance is to be registered as provided by By-Laws changes, we desire to make our Annual Meeting outstanding as reward rather than routine. The program will be announced at an early date.

The Orientation Dinner and Indoctrination Ceremony for Provisory members held on January 20, 1966, was described to the Board as most rewarding to all participants.

Life membership was granted to Dr. Henry Giamarino after 42 years of membership.

The next meeting will be held on February 24, 1966 at 4:30 P.M. at the Colonial House.

### **From The Connecticut State Department Of Health**

The Connecticut Council for Planning Hospital and Medical Facilities today reviewed and approved the 1966 revision of the statewide plan for the program, it was announced by Franklin M. Foote, M.D., Commissioner, Connecticut State Department of Health. He said that an entirely new system of priorities for U. S. Public Health Service grants had been made a part of the 1966 revision.

This year's plan, under which approximately \$2,000,000 will be distributed, incorporates changes in methods of determining the need for hospital, nursing home and public health centers, and other medical facilities in accordance with the requirements of federal Public Law 88-443.

One of the changes effected by the passage of this law was to provide funds for the modernization of hospitals and medical facilities. The needs for such modernization in Connecticut has been determined in this year's plan. Another change will virtually eliminate new construction of religious sponsored and non-profit nursing homes with the help of federal funds.

Dr. Foote explained that the council decided to retain the same 11 hospital service areas as last year and to establish 4 priority groups for each category of facility for both new construction and modernization. The priorities are used in determining allocation of federal grants to assist in constructing or modernizing medical facilities. These grants are available to sponsors of eligible non-profit projects which serve a community need and have admission policies unrestricted as to race, color or religion.

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## ANNUAL MEETING OF THE WOMAN'S AUXILIARY TO THE CONNECTICUT STATE MEDICAL SOCIETY

**Wednesday, April 27, 1966**

**The Corner House, Farmington, Conn.**

**Save The Date**

The 22nd Annual Meeting of the Woman's Auxiliary to the Connecticut State Medical Society will be held on April 27th, 1966, at The Corner House in Farmington, Conn.

Registration will be at 10:00 A.M., with the business meeting at 10:30 A.M.

Dr. Francis Gallo, Chairman of the Board of COMPAC will address the members at the business meeting.

There will be a hospitality hour from 12:00 to 1:00 with luncheon at 1:00. At the luncheon, Mrs. Karl F. Ritter of Lima, Ohio, a national director of the Woman's Auxiliary to the American Medical Association will speak.

### DATES TO REMEMBER

*Annual Convention of WAAMA*, June 26-30, 1966, at the Drake Hotel, Chicago, Illinois.

*Annual Conference of WAAMA*, October 2-5, 1966, at the Drake Hotel, Chicago, Illinois.

*Regional Workshop*, Eastern Region, New York, 1966, October 10-11, (hotel to be announced). The Regional Workshop will be for the following State Committees: AMA-ERF, Community Service, Legislation, Membership, Mental Health, Rural Health.

November, 1966—Clinical Conference of the AMA will be held in Las Vegas, Nevada.

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### Which Son Will Be A Doctor?

If you aspire to have a doctor in your family, your eldest son may turn out to be the one who aims for a medical career.

The eldest may be most likely to enter medical school, particularly if he has several brothers and sisters, or if his father didn't achieve quite the status that could be expected from the father's level of education.

These are some of the preliminary findings of a report in the current Journal of the American Medical Association.

The report is by two staff members of the Institute for Social Research at the University of Michigan. It is based on a survey of the class of 1968 at the university's School of Medicine.

When the 207-member class entered medical school in fall 1964, it contained 2½ times as many eldest sons of families as youngest sons, the report said. (The report actually is based on a study of 172 male students who had brothers or sisters. The class also contained 11 women and 20 men who were only children. Four students were absent at the time of the survey.)

The unusual frequency of eldest sons as medical students was "particularly striking" for families in which the father's occupation is "low in the socioeconomic scale relative to his education," the authors said.

They suggested that fathers who fail to achieve some of their own ambitions may strongly influence the aspirations of their sons.



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## OBITUARY

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### **William J. Bodie, M.D.**

**1897 - 1965**

Dr. William Joseph Bodie of Branford, Connecticut, died in the Hospital of St. Raphael on December 21, 1965. Death was due to multiple myeloma and pneumococcus meningitis.



Dr. Bodie was the son of the late John and Marie McKeon Bodie. He was born in New Haven and attended Sacred Heart School, Hillhouse High School in 1918 where he played on the baseball and football teams with distinction. He was graduated in 1925 in the first graduating class of Providence College, where he played on the baseball team. He graduated in 1929 from Georgetown Medical School in Washington and served his internship at the Hospital of St. Raphael from 1929 to 1930.

Dr. Bodie practiced general medicine in Branford from 1931-1962 when he became ill. He served as assistant attending in medicine at the Hospital of St. Raphael from 1933 to 1962.

Dr. "Bill" served in the Navy in World War I and as a Major U.S.M.C. from 1942 to 1945, during which service he was awarded the Bronze Star and Special Commendation Medal for Outstanding Service Beyond the Call of Duty.

Providence College rewarded him a degree of Honorary Master of Science in 1963.

Dr. Bodie leaves his wife, Mrs. Rebecca Glazer Bodie, a daughter, Mrs. Rebecca Bomster, and a son William J. Bodie, Jr., his brother Dr. John A. Bodie of New Haven, and five grandchildren.

Dr. "Bill" Bodie was blessed with a fine physique, was noble in appearance, possessed a gentle and

kindly manner. He was observant and tolerant. He had spent several years in the seminary prior to deciding upon medicine as a career, thus being exceedingly well prepared to meet the vicissitudes of life and the variations of his fellow men in a most philosophical manner.

He was the ideal practitioner in general practice, beloved and respected by his patients and his community and highly regarded by his colleagues who looked upon him as a gentleman in the practice of medicine. Requiescat in pace.

ALBERT J. HOWARD, M.D.

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## In Memoriam

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**Dennehy, William J.**—New Haven; Yale School of Medicine, 1918. Dr. Dennehy had practiced medicine in New Haven for 40 years. During World War I, he served as a lieutenant in the Navy. He was a member of the staff of the Hospital of St. Raphael. He was a member of the Connecticut State Medical Society and the American Medical Association. He was also a member and past secretary of the New Haven County Medical Association. Dr. Dennehy died January 31, at the age of 70.

**Garlick, George B.**—Fairfield; Yale School of Medicine, 1912. Before retiring in 1958, Dr. Garlick had been an ear, nose and throat specialist in the Fairfield area for 44 years. During World War I, he served in the Medical Corps as a First Lieutenant. Dr. Garlick was a member of the Bridgeport Medical Association, the Fairfield County Medical Association, the Connecticut State Medical Society, and the American Medical Association. Dr. Garlick died February 1, at the age of 80.

**Giamarino, Henry J.**—New Haven; Baltimore University School of Medicine, 1906. Dr. Giamarino was a veteran of World War I and a practicing surgeon in the New Haven area for more than 54 years. He was a member of the Courtesy Surgical Staff at Yale-New Haven Hospital, the American and International Colleges of Surgeons, the New Haven County Medical Association, the Connecticut State Medical Society, and the American Medical Association. Dr. Giamarino died February 10, at the age of 83.

## Special Notices

### YALE MEDICAL SOCIETY SYMPOSIUM

Tuesday, March 15th

4:30 P.M.

Mary S. Harkness Auditorium  
Sterling Hall of Medicine  
333 Cedar Street, New Haven

"Of All Female Teenagers in Connecticut in 1965, One Out of Six was Illegitimately Pregnant. Is There a Solution?"

Panel Members:

Dr. George James, Dean, Medical College of Mount Sinai Hospital, New York

Dr. Stephen Fleck, Department of Psychiatry, Yale University School of Medicine

Dr. Philip Sarrel, Department of Obstetrics and Gynecology, Yale University School of Medicine

### KIDNEY FOUNDATION OF CONNECTICUT

March 30, 1966

The Kidney Foundation of Connecticut, an affiliate of the National Kidney Foundation, announces the Second Symposium on Kidney Disease at the Mary S. Harkness Auditorium, Yale University, 333 Cedar Street, New Haven, Connecticut, Wednesday, March 30th, 1966. Program sessions 9:00 A.M. to 5:00 P.M. Registration Fee \$5.00. This includes luncheon. Courtesy registrations (do not include luncheon) are available for house staff, research fellows and nurses upon request from their supervisor. The current status of kidney transplantations and the management of chronic renal diseases will be included in the program.

### ANNUAL MEETING OF THE CONNECTICUT

DIABETES ASSOCIATION

April 27, 1966

Dr. Martin G. Goldner, Professor of Medicine at State University of New York and Director of the Department of Medicine at the Jewish Hospital of Brooklyn, will speak at the Annual Meeting of the Connecticut Diabetes Association on Wednesday, April 27 at 3:30 P.M. at the Statler Hotel in Hartford.

His topic will be "Drug Management of Organic Hypoglycemias."

### SYMPOSIUM ON MODERN TRENDS IN MIDDLE EAR SURGERY

Newark, New Jersey

Wednesday, May 18, 1966

The Academy of Medicine of New Jersey and the New Jersey Academy of Ophthalmology and Otolaryngology will present a one day program on current trends in middle ear surgery. Topics include endolymphatic sac surgery, Meniere's disease, acoustic neuroma, complications of stapes surgery, progress in middle ear microsurgery, and inner ear pathology associated with chronic otitis media and mastoiditis. The speakers will be Dr. J. Brown Farrior, Dr. Frederick R. Guilford, Dr. Harold F. Schuknecht, and Dr. George E. Shambough.

Registration fee of \$10 should be sent to Academy of Medicine of New Jersey, 317 Belleville Avenue, Bloomfield, New Jersey before May 1, 1966.

## Doctor's Office

Beverly A. Foss, M.D., announces the opening of an office for the practice of obstetrics and gynecology at 159 Ocean Avenue, New London.

Joseph M. Gromults, Jr., M.D., announces the opening of an office for the practice of internal medicine at 668 Post Road, Darien.

John W. Haine, M.D., announces the removal of his office to 83 Morgan Street, Stamford.

William A. Sinton, M.D., Robert P. Fornshell, M.D., and Felix J. Callan, M.D., announce the association of Francis P. Saunders, M.D. in the practice of orthopedic surgery at 85 Osborne Street, Danbury.

Robert Turfboer, M.D., announces the removal of his office for the practice of psychiatry to 300 Amity Road, Woodbridge.

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## SYMPOSIUM

### ADVANCES IN THE DIAGNOSIS OF MALIGNANCY

**Wednesday, April 13, 1966**

The New Haven Branch of the American Cancer Society, in association with the Academy of General Practice, New Haven Branch, are presenting a one day symposium on Advances in the Diagnosis of Malignancy on Wednesday, April 13, 1966, from 9:00 A.M. to 3:00 P.M. at the Education Building, Hospital of St. Raphael, New Haven.

The speakers will be Simon Berger, Philadelphia; Burton Lee, New York; Merrill Bender, Buffalo, New York, and Averill Liebow of New Haven. Topics will include cytologic techniques, mammography, thermography, isotope techniques, and lymphangiography.

There will be no registration fee and the meeting is open to all physicians.

If Ben Franklin were alive today he would say:

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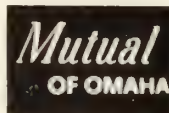
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## NEW BOOKS IN REVIEW

**HYPERTENSION. Vol. 13. *Proceedings of the Council for High Blood Pressure Research. American Heart Assoc. Cleveland. November 13-14, 1964. Edited by Simon Rodbard, M.D. 200 pp. Illustrated. \$2.50.***

Reviewed by: LOUIS H. NAHUM

There are 43 contributors of high standing in the basic science field to this issue and 14 original contributions divided into three sections, each followed by a spirited discussion.

The first group of papers deal with such studies as renal tissue fluid turnover, uptake, storage release and metabolism of catecholamines by the heart, metabolism of nor-epinephrine in patients with hypertension, inter-relationship between elevation of blood pressure and angina pectoris, and the action of nor-epinephrine and nerve stimulation on a perfused foreleg of the dog.

The second group of papers are devoted to the renin-angiotensin system and their actions.

The third group is made up of five papers dealing with peripheral circulation, auto-regulation, capillary circulation, and the calcium control of the arterial wall in normotensive and hypertensive rats.

This symposium is obviously by and for physiologists with the relation of the findings to clinical hypertension somewhat unclear. As is true of basic science in general, it is hoped that out of it will come some practical benefits that the physician will be able to use in understanding and managing the hypertensive patient.

A paper on primary aldosteronism and how it produces hypertension would have belonged in this symposium and would have been of practical value also to the clinician as well as the physiologist.

***SURGERY IN WORLD WAR II, THORACIC SURGERY, Volume II. Prepared and published under the direction of Lieutenant General Leonard D. Heaton, The Surgeon General, United States Army. Office of the Surgeon General, Department of the Army, Washington, D.C., 1965. Illustrated.***

Reviewed by: C. ELTON CAHOW

Few areas of endeavor derive lasting benefit from war. Surgery, and thoracic surgery in particular, are exceptions to this rule. The principles governing thoracic surgery gained impetus during World War I. Thereafter, progress was surely but at times painstakingly slowly achieved. With the advent of World War II, advances in the understanding of basic pathophysiologic concepts and the development of technics based on these concepts were tremendously accelerated. This did not happen by chance but occurred as a result of very careful interpretation and analysis of the data accumulated from battle casualties. As in volume I, the authors of this second volume on Thoracic Surgery in World War II present the results of their cumulative experience in the Mediterranean and European theaters of operation and in the Zone of Interior.

The book is divided into three sections. In section I, "Special Types of Wounds of the Chest," thoracic, cardiac and thoracoabdominal wounds are considered in detail. The material is presented in a straightforward factual manner, including pertinent case material illustrative of each type of wound. Of special interest in this section is the discussion of wounds of the heart, including retained foreign bodies. Newer concepts in management of these wounds are discussed in detail.

In section II, "Complications of Wounds of the Chest," special attention is devoted to "certain complications of these injuries whose significance was realized, or fully realized, for the first time in World War II." These complications include the "wet lung" syndrome, hemothorax and hemothoracic empyema. The natural history of traumatic hemothorax as it progresses to thrombosis and organization or develops into hemothoracic empyema is clearly described. In addition, pertinent histologic sections are reproduced to illustrate these changes. The authors then proceed with a well-grounded discussion of the necessity for and the timing of decortication in these cases. The successful removal of retained foreign bodies from the heart and great vessels at 134 operations without a mortality constitutes a remarkable surgical accomplishment.

Section III, "Observations on Wounds and Diseases of the Chest in the Zone of Interior," includes the more complicated cases from the battle zones as well as the pulmonary diseases ordinarily encountered in any large population. An especially interesting feature of this section is the 15-18 year followup and re-evaluation of 167 patients who sustained thoracic trauma during 1943-45. The good end results in this small group substantiates the sound reasoning upon which therapy was based.

The tremendous volume of material encompassed by these authors represents an editorial accomplishment worthy of praise. That this material is well organized, thoroughly digested and presented in a comprehensive manner is further reason to consider this work one of the more significant contributions to the surgical literature. If at times the authors seem repetitive and didactic this is a minor fault of a book which is otherwise so well written.

***TEXTBOOK OF OBSTETRICS. Authors: John C. Ullery; Zeph J. R. Hollenbeck. The C. V. Mosby Company, Saint Louis 1965, 752 pp. with 292 fig. and 3 color plates. \$17.50.***

Reviewed by: ORVAN W. HESS

This guide for the care of obstetrical patients is a product based on the abundant clinical experience of members of the Department of Obstetrics and Gynecology at Ohio State University School of Medicine. It is augmented by contributions from others representing several closely related disciplines. In accordance with a presently prevailing concept among medical educators, the objective of the book is an attempt to supply students at all levels with insight concerning methods of arriving at the solution of problems of man-

agement rather than to furnish a didactic outline to be dutifully followed for the treatment of disease entities.

Presentation of clinical material concerned with a particular subject under discussion is correlated with pertinent anatomical, physiological and pathological considerations. This is done in such a manner as to effectively provide a logical explanation for the management of a wide variety of conditions which may be encountered in either private practice or a hospital environment.

This 752 page textbook is very readable and should be of great practical value to practitioners.

#### **CELLULAR BIOLOGY OF MYXOVIRUS INFECTIONS.**

*Edited by G. E. W. Wolstenholme and Julie Knight.*

*Ciba Foundation Symposium. Little, Brown and Co., Boston, Massachusetts, 1964. 368 pp. \$12.00.*

Reviewed by: PETER ISACSON

Influenza was one of the first well-studied animal viruses since it grows readily in embryonated eggs and can be easily assayed by hemagglutination. Up to 1950 most texts on animal virology were primarily concerned with influenza and the related mumps and Newcastle Disease viruses; there was simply little else to discuss. Then tissue culture appeared on the scene and allowed for precise quantitative techniques in the study of many other animal viruses. Orientation in basic research shifted markedly towards the simpler animal viruses such as poliovirus. Aside from the availability for research tools, this shift was aided by the extensive grant support of the National Foundation for Infantile Paralysis.

In this process myxoviruses lost much of their attention. In the past few years, however, there has been a resurgence of interest in myxoviruses for reasons well illustrated by this symposium. To begin with, this family of viruses has considerably enlarged and now includes parainfluenza viruses 1-4, measles, rinderpest, distemper, and RS (respiratory syncytial) as well as the previously mentioned influenza, mumps, and Newcastle disease viruses. Secondly, myxoviruses are chemically and structurally complex and pose many fascinating questions. In contrast to the simple viruses which are composed solely of nucleic acid covered by symmetrically arranged viral protein subunits, myxoviruses contain an inner ribonucleoprotein helical core surrounded by an envelope through which spikes project. The envelope contains lipids, enzymes, and a variety of incorporated preformed host macromolecules, including host antigens. Aside from the ability to infect host cells, these viruses have the biological features of hemagglutination, internal and external antigens, and some possess the enzyme neuraminidase as well as a hemolysin and cell-fusion factors. Virologists who were at first dismayed by the complexity of these viruses are now realizing that a correlation of structure and function in myxoviruses will be of considerable importance in understanding host-parasite relationships to a level somewhat more involved than represented by the simple viruses.

This symposium brings together the pertinent recent advances in the areas of structure, classification, intracellular development, genetics, and antigenic composition of myxoviruses. There are fourteen contributions by leading workers in the field with discussions after each article. Although not in the format of journal articles, most are presentations of

original data from the authors' own laboratories, rather than serving as literature reviews. There is the inevitable unevenness of style but the majority of the presentations are clear, concise, and valuable contributions.

The appeal of this symposium will be largely limited to those actively engaged in laboratory research in animal virology. This is the audience for whom it was intended and there is no pretense at developing any direct implications to clinical disease. For anyone with more than superficial interest in infectious disease, however, this collection will give valuable insight into the trends of fundamental research on myxoviruses.

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## BOOKS RECEIVED

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*Books received for review are acknowledged in this department and such acknowledgement must be regarded as a sufficient return for the courtesy of the sender. Selection will be made for review in the interests of our readers and as space permits.*

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*Index-Handbook of Cardiovascular Agents* Volume 3 (1956-1959) Isaac D. Welt, Ph.D., Published for The Institute for Advancement of Medical Communication. The Blakiston Division. McGraw-Hill Book Company, Inc., New York, Toronto, Sydney and London \$32.50.

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*Geriatric Psychiatry: Grief, Loss, and Emotional Disorders in the Aging Process.* The Boston Society for Gerontologic Psychiatry, Inc. Edited by Martin A. Berezin, M.D. and Stanley H. Cath, M.D. International Universities Press, Inc., New York \$7.50.

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*Current Pediatric Therapy 1966-1967.* Sydney S. Gellis, M.D. and Benjamin M. Kagan, M.D. W. B. Saunders Co., Philadelphia and London, 1966. 956 pp. \$17.50.

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*Death And Dying: Attitudes Of Patient And Doctor.* Group for the Advancement of Psychiatry. Symposium No. 11. Volume V. 80 pp. \$1.50.

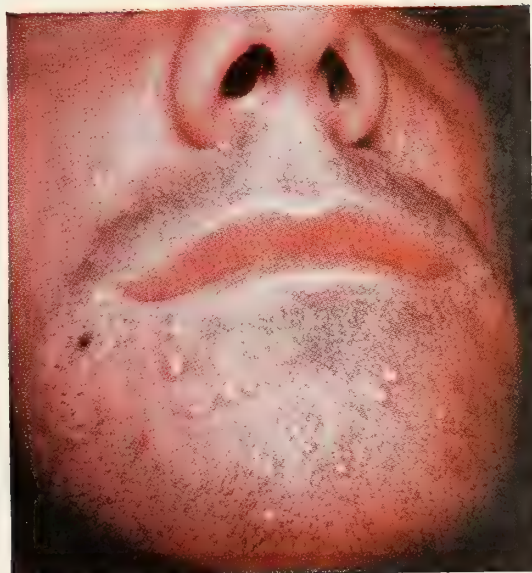
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*The Cell, Its Organelles and Inclusions.* An Atlas of Fine Structure. Edited by Don W. Fawcett, M.D. W. B. Saunders Co., Philadelphia and London, 1966. 448 pp. \$11.00.

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*Gonadotropins: Physicochemical and Immunological Properties.* Ciba Foundation Study Group No. 22. Edited by G. E. W. Wolstenholme, O.B.E. and Julie Knight, B.A. Little, Brown and Company, Boston, 1955. 125 pp. with 28 illustrations. \$3.50.

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*Man and Africa.* A Ciba Foundation Symposium jointly with The Haile Selassie I Prize Trust under the patronage of His Imperial Majesty Haile Selassie I Emperor of Ethiopia. Edited by Gordon Wolstenholme and Maeve O'Connor. Little, Brown and Co., Boston, 1965. 400 pp. with 24 illustrations. \$7.50.

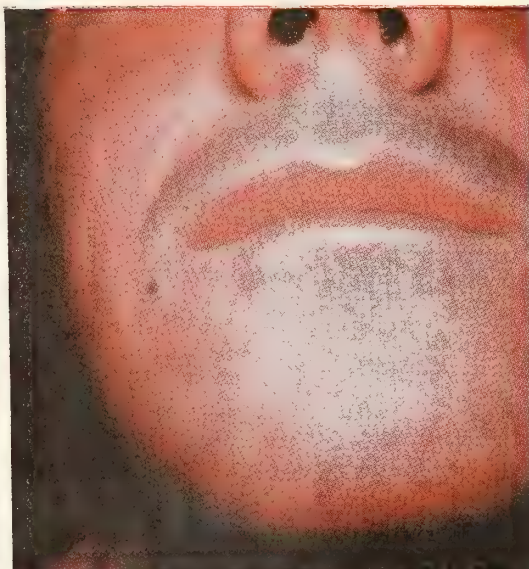


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**Caution:** As with other antibiotic preparations, prolonged use may result in overgrowth of nonsusceptible organisms and/or fungi. Appropriate measures should be taken if this occurs.

**Contraindication:** This product is contraindicated in those individuals who have shown hypersensitivity to any of its components.

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### AMA Nutrition Lectures Presented At Two Connecticut Colleges

The Connecticut State Medical Society, in cooperation with the American Medical Association and two Connecticut county medical associations sponsored clinical nutrition lectures in two colleges during the month of March.

Dr. Nevin S. Scrimshaw, Professor and Head of the Department of Nutrition and Food Science, Massachusetts Institute of Technology, delivered the lectures, both on the topic of "Food and Nutrition in the Future."

The lectures were presented at the Willimantic State College, Willimantic, on March 3, in cooperation with the Windham County Medical Association, and at Quinnipiac College, Hamden, with the cooperation of the New Haven County Medical Association on March 15.

Designated staff personnel of area hospitals, schools, and convalescent homes were invited to attend the lectures.

The AMA's Council on Foods and Nutrition initiated the clinical nutrition program during the last academic year and it is being carried out in regions of the United States with several prominent lecturers participating.

The lectures are planned to stimulate undergraduate students to consider careers in the health sciences and to inform physicians and health personnel of new developments in nutrition.

Thirty-six lectures have been scheduled in the four-state region which includes Connecticut, New York, Ohio, and Pennsylvania.

### Athletes Warned About Drugs

An American Medical Association committee today warned athletes and coaches that unauthorized use of two types of drugs in sports carries serious health risks.

The drugs are DMSO (dimethylsulfoxide), the highly publicized solvent and "pain reliever" that is still in the testing stage, and androgenic-anabolic steroids, which are sometimes used with the hope of inducing weight gain.

Use of these drugs has apparently been creeping into athletics, said the AMA Committee on the Medical Aspects of Sports. Both types of drugs are completely inadvisable for athletes, as are the amphetamines (pep pills) about which previous warnings have been issued.

#### Androgenic-Anabolic Steroids

"There is no excuse for giving (these steroids) to healthy athletes of any age," the committee said.

"These drugs are categorically condemned for the athlete. Any drug sufficiently potent to alter the body's metabolism is sufficiently potent to have undesirable as well as desirable effects."

In prepubertal boys, the committee said, the steroids may prematurely stop growth, induce precocious puberty, and result in decreased testicular size. In the pubertal boy, the steroids markedly suppress production of testosterone, a male hormone, in the developing testes. In adult males, testicular size and function revert to the prepubertal stage, and there is "decreased libido," the committee said. Oral doses of the steroids have produced changes in liver function in all age groups.

If these effects aren't enough to discourage use of the "weight-gain" steroids, the committee said athletes should consider that a recently completed study showed no significant performance differences between athletes who received an anabolic steroid and others who received a placebo, or "blank."

The androgenic-anabolic steroids are so named because they resemble, chemically and functionally, the male sex hormones. Male (androgenic) hormones are produced primarily by the testes; testosterone is the principal androgen. All the commercially available androgenic steroids share the properties of testosterone, which are (1) growth stimulation, (2) acceleration of bone maturation, and (3) virilization.

It is true that androgenic-anabolic steroids may lead to increased weight. These drugs also have other benefits that make them useful in the treatment of some anemias, osteoporosis of bone, and chronic debilitating illnesses, as well as male hormone deficiencies.

However, when the drug consumer is a healthy male without deficiencies, significant new problems are posed. The ill effects, such as decrease in ultimate height, decreased testicular size, and changes in liver function, are insidious and not immediately apparent, the AMA committee said.

#### DMSO

As for DMSO, the problem is that "popular publicity jumped the gun on the necessary testing procedures established by law to protect the public," the committee said. "A public demand for DMSO's purported sensational qualities has reached the physician long before sound scientific investigations can define its values and hazards."

DMSO is an old chemical solvent that is being investigated as a drug. Currently, its only legal ethical use is by physicians in registered studies with several sponsoring drug companies. This status of DMSO—for sports or other uses—will not



change until the U. S. Food and Drug Administration releases it for stipulated clinical purposes, or declares it ineffective or too hazardous for use.

Compounding the problem is that there are two grades of DMSO, the medically pure grade, which is under test, and readily available industrial-grade solvent, which contains impurities.

The DMSO that would be used on an athlete by anyone other than a physician in a registered study would be the impure industrial grade. (If promoted otherwise, the promotion is fraudulent or stolen goods are being used.)

DMSO is a potent solvent and penetrating agent, and is even a carrier of other agents through the skin. Whatever impurities are dissolved in the industrial-grade DMSO could be absorbed in the body.

Even when medically pure DMSO is used, an athlete might also absorb toxic "external use only" ingredients of commonly used medicinal products. Insecticides and other chemicals sprayed on a football field might be carried into a player's blood stream by DMSO and cause serious side effects.

"With some chronic conditions, pain relief is undoubtedly a benefit. But in sports, pain is a respected safeguard against the premature return of the athlete to competition," the AMA committee said.

Using DMSO to mask pain so that an athlete can return to activity may cause a serious injury or health problem to be overlooked. It also might result in further abuse of the injury.

"Athletes, coaches, trainers, and team physicians should depend only upon products, practices, and resources known and proven to be of help in reaching and maintaining optimal performance levels—before and after injury.

"By doing so, they are safeguarding the health of the athlete as well as assuring peak performance," the committee said. "Improper or doubtful care of the injured athlete does him no service; it merely leads to aggravation and extended absence from peak performance if not in fact to the obliteration of future goals. This should be enough to prevent anyone devoted to athletics from trying unproven drugs such as DMSO."

### Married Couples Strike A Bargain

To make their marriages work, many middle-class American husbands and wives strike long-term "bargains" with each other, suggests an article in the current Archives of General Psychiatry, published by the American Medical Association.

These agreements often have little to do with commonly recognized sexual roles, said Don D. Jackson, M.D., director of the Mental Research Institute, Palo Alto, Calif.

The quid pro quo ("something for something") relationships are simply a way to work out the running of a household.

One of the most common arrangements, Dr. Jackson said, is one in which the husband is "an instrumental type who deals with matters logically and intellectually, and is considered the practical, realistic one. His wife is the more sensitive, affective or 'feeling' sort of person who understands people better than things."

But there are other arrangements. One is a "time bound" relationship:

"The husband may suggest to his wife that they go to a movie; she says yes, and then she has the right to say, we can have a beer afterwards. Similarly, the wife may take certain rights which the husband will grant because he knows he will have a turn in the near future."

Dr. Jackson said there also is a peculiar relationship which can be observed in both marital and political situations, "when the quid pro quo is not time-bound, but is treated as if it is.

"If A says to B, let us do X, B says yes because A indicates that eventually B will get his reward. B's day is allegedly coming, and though it never does, A keeps acting as if it is going to and B keeps acting as if he accepts this."

These are often pathological relationships which in marriage are frequently characterized by depression and even suicide.

"The vicious cycle aspect of this relationship is apparent—the more B lets himself be conned, the more he has coming eventually and the less free he is to try another game, since he has so much already invested," the report said.

Still another tactic is "one down" behavior:  
Husband: I wish you would fix yourself up.  
Take \$50 and get a permanent, a facial—the works!

Wife: I'm sorry dear, but I don't think we ought to spend the money on me.

Husband: \*&%#! I want to spend it on you!

Wife: I know dear, but there are all the bills and things. . . .

"If we look beyond the particular \$50 about which they are disputing, we can see the relationship they have worked out," the report said.

"The husband is allowed to complain about the wife and act in charge, but the wife indicates she does not intend to follow his orders, that in fact his orders are stupid and, since she sets no time conditions, we do not know if she will ever get a permanent or not.

"This is one clue to the quid pro quo. Rather than executing a piece of action, this couple is going through a repetitive exchange which defines and redefines the nature of their relationship."

It's possible that the formulation of "rules" such as the quid pro quo has "enormous predictive potential," the report said. "If we are reasonably accurate in our formulation of a metaphor for a couple's relationship, we can forecast the likelihood of success or failure (of the marriage) and even the fate of children in the family system."

### Special Report On Pollution

Our increasingly dirty skies, polluted water, and mounting piles of rubbish are health problems that must be solved soon, says the current *Today's Health* magazine.

The magazine, published by the American Medical Association, devotes most of the issue to a special report on pollution and environmental health.

Air pollution, one article noted, is subtly affecting everything we buy and do, yet we are not using all the available tools to combat it.

We're learning more about re-using waste water, but water pollution is robbing us of one of the elements most vital to existence, two articles say.

Another article tells how engineers are studying ways to reuse the thousands of tons of rubbish created in this country every day. Some can be used as heating fuel, some goes into useful sanitary landfills, and some metal waste can be salvaged. Getting rid of rubbish, however, is a mounting headache. Americans are throwing away 800 million pounds of it every day; collecting and disposing of it costs more than \$1.5 billion a year.

Other articles tell of the continuing scientific effort to assure the safety of chemically treated food, and of the growing interest in the relationship of trace metals to nutrition.

Our national planning for conservation involves a struggle between the "preservationists" and the "utilizationists," says an article by Hal Higdon. The public, caught in the middle, has a right to ask for a workable national plan, the article says.

The special issue of *Today's Health* precedes the AMA's first Air Pollution Medical Research Conference, March 2-4 at the Ambassador Hotel, Los Angeles.

Six other medical and health organizations are cooperating with the AMA in the conference on air pollution and chronic respiratory diseases. They are the American College of Chest Physicians, the American Thoracic Society and the U.S. Public Health Service, the California Department of Public Health, California Medical Association, and the Los Angeles County Medical Association.

The third AMA Congress on Environmental Health Problems, concentrating on the impact of environment on accidental injuries and fatalities, will be April 4-5 at the Drake Hotel, Chicago.

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**Contraindications:** Benactyzine hydrochloride is contraindicated in glaucoma. Previous allergic or idiosyncratic reactions to meprobamate contraindicate subsequent use.

**Precautions:** *Meprobamate*—Careful supervision of dose and amounts prescribed is advised. Consider possibility of dependence, particularly in patients with history of drug or alcohol addiction; withdraw gradually after use for weeks or months at excessive dosage. Abrupt withdrawal may precipitate recurrence of pre-existing symptoms, or withdrawal reactions including, rarely, epileptiform seizures. Should meprobamate cause drowsiness or visual disturbances, the dose should be reduced and operation of motor vehicles or machinery or other activity requiring alertness should be avoided if these symptoms are present. Effects of excessive alcohol may possibly be increased by meprobamate. Grand mal seizures may be precipitated in persons suffering from both grand and petit mal. Prescribe cautiously and in small quantities to patients with suicidal tendencies.

**Side effects:** Side effects associated with recommended doses of 'Deprol' have been infrequent and usually easily controlled. These have included drowsiness and occasional dizziness, headache, infrequent skin rash, dryness of mouth, gastrointestinal symptoms, paresthesias, rare instances of syncope, and one case each of severe nervousness, loss of power of concentration, and withdrawal reaction (status epilepticus) after sudden discontinuation of excessive dosage.

*Benactyzine hydrochloride*—Benactyzine hydrochloride, particularly in high dosage, may produce dizziness, thought-blocking, a sense of depersonalization, aggravation of anxiety or disturbance of sleep patterns, and a subjective feeling of muscle relaxation, as well as anticholinergic effects such as blurred vision, dryness of mouth, or failure of visual accommodation. Other reported side effects have included gastric distress, allergic response, ataxia, and euphoria.

*Meprobamate*—Drowsiness may occur and, rarely, ataxia, usually controlled by decreasing the dose. Allergic or idiosyncratic reactions are rare, generally developing after one to four doses. Mild reactions are characterized by an urticarial or erythematous, maculopapular rash. Acute nonthrombocytopenic purpura with peripheral edema and fever, transient leukopenia, and a single case of fatal bullous dermatitis after administration of meprobamate and prednisolone have been reported. More severe and very rare cases of hypersensitivity may produce fever, chills, fainting spells, angioneurotic edema, bronchial spasms, hypotensive crises (1 fatal case), anuria, anaphylaxis, stomatitis and proctitis. Treatment should be symptomatic in such cases, and the drug should not be reinstituted. Isolated cases of agranulocytosis, thrombocytopenic purpura, and a single fatal instance of aplastic anemia have been reported, but only when other drugs known to elicit these conditions were given concomitantly. Fast EEG activity has been reported, usually after excessive meprobamate dosage. Suicidal attempts may produce lethargy, stupor, ataxia, coma, shock, vasomotor and respiratory collapse.

**Dosage:** Usual starting dose, one tablet three or four times daily. May be increased gradually to six tablets daily and gradually reduced to maintenance levels upon establishment of relief. Doses above six tablets daily are not recommended even though higher doses have been used by some clinicians to control depression and in chronic psychotic patients.

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## What Cures Acne?

Acne, the old scourge of teenage complexions, may be helped as much by the patient's cordial relationship with his doctor as by treatment with antibiotics.

That's one of the findings of research reported in the current *Journal of the American Medical Association*.

Tests of two antibiotics on 45 college and nursing students showed that their skin troubles came and went irregularly, seemingly regardless of whether drugs were administered.

Sometimes a patient's skin cleared up when all he or she had been given was a placebo, or dummy capsule. In fact, "significant improvement" was noted in 24 per cent of patients when given placebos.

"It is clear that sympathetic and enthusiastic physician-patient relationships can markedly benefit many acne patients even in the absence of active medication," said the author of the report, Robert G. Crounse, M.D., of the University of Miami School of Medicine, Coral Gables, Fla.

As for the antibiotics, Dr. Crounse said results of his study do not support the use of systemic antibiotics in treating acne vulgaris. This varies with the widely held belief that antibiotics are an effective acne treatment, he said.

In his investigation, there were no significant statistical differences in results obtained with one or the other of the antibiotics or the placebos, Dr. Crounse said.

Although some good results were obtained with one antibiotic, demethylchlortetracycline, Dr. Crounse urged caution in interpreting these. In 8 of 15 "excellent" and "good" responses to antibiotic treatment, the patients developed undesirable photoreactivity to sunlight. The other antibiotic tested was tetracycline hydrochloride.

The relatively high cost of antibiotics, their frequent ineffectiveness, and the occasional dangers of

sensitization should be weighed in treating each individual patient, Dr. Crounse said.

## Mutilation Or Prophylactic Surgery?

In his many years of medical practice in northern Morocco, Charles A. Apffel, M.D., met many patients who had no uvula, the fleshy pendant at the back of the soft palate.

He discovered that the ancient custom of surgical removal of the uvula in early childhood persists among certain Moroccan tribes.

Dr. Apffel made another discovery: in none of more than 200 persons on whom the operation had been performed could he see or feel any trace of tonsils or adenoids. The child's regional lymphoid tissue simply doesn't develop after the operation, he concluded.

"Such individuals may contract a diffuse pharyngitis, but never a tonsillitis or adenoiditis," Dr. Apffel writes in the current *Journal of the American Medical Association*.

Uvulectomy's bearing on reduction of rheumatic fever or chronic arthritis can only be suspected, Dr. Apffel said. However, eliminating the uvula gets rid of one center of infection, he pointed out.

Uvulectomy, as practiced in northern Morocco, has no religious motivation and is not related to any of the rites enjoined in the Koran, Dr. Apffel said. It is transmitted from generation to generation as a family tradition. It is meant to aid breast feeding and speech.

The operation is customarily performed by the sexton of the neighborhood mosque, or by a barber. Many Moroccan barbers still act as practical surgeons.

"Whatever the consequences of neonatal uvulectomy, they point to a close interdependence between the uvula and the constituents of the Waldeyer ring (the adenoidal tissue formed by the lingual, pharyngeal, and faucial tonsils)," Dr. Apffel said.

He suggested that the custom may have originated in the ancient Spanish medical schools, and then been transferred to northern Morocco when the Moors were forced out of Spain.

Dr. Apffel is on the staff of Pondville Hospital, Walpole, Mass.

## The Wonderful World Of Drug Serendipity

Serendipity has always provided some of the greatest discoveries. Search for a seasickness remedy produced the antihistamines. Investigation of a hiccup remedy yielded a potent analgesic. Subse-



quently, the antihistamines were discovered to be antinauseants; then tranquilizers. Snake venoms, studied for the treatment of arthritis, were found to be anticoagulants and fungicides. The combined study of antibacterial drugs and cabbage feeding led to the antithyroid drugs. From these, it can be seen that the ultimate destiny of a new drug is not always predictable until its use is widespread.—A. Lee Lichtman, M.D., in *Experimental Medicine and Surgery*, 22:2-3 (Jun.-Sep.) 1964.

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### **Within 5 Years—14 New Medical Schools**

Fourteen new medical schools are expected to be in operation in the United States by 1970.

These will bring to 101 the nation's total of schools of medicine, and mark an "era of major expansion" in American medical education, said the current *Journal of the American Medical Association*.

"Of obvious and immediate importance is the fact that 800 to 1,000 new positions will be available to qualified medical applicants," the *Journal* said. "This will help to meet the urgent national need for more physicians."

In addition to these 14 firm commitments to build schools, at least 10 other institutions "seem to be reasonably good possibilities to follow through with the development of a new (medical) school," the *Journal* said.

The new medical schools are but one of the indicators that American medical education is expanding.

The 65th annual report on medical education by the AMA's Council on Education is published in the current issue of the *Journal*. The report contains data which mark continuing gains in graduate medical education, continuing medical education, educational programs in areas allied to medicine, and programs of government agencies pertinent to medical education.

All of the new medical schools will introduce modifications of the standard medical curriculum. This should lead to "some very interesting experiments in medical education," the *Journal* said.

The new schools also will be competing for faculty with existing schools.

"This will certainly aggravate an existing manpower problem, but it will also open up new opportunities for leadership to young, vigorous medical scientists," the *Journal* said.

Over the past 20 years, the number of medical schools has increased steadily from 77 schools in 1945 to 88 in 1965. The next five years, however, will mark the period of greatest expansion.

Eight of the 14 schools being planned will provide full four-year programs leading to the M.D. degree. The other six are envisioned as two-year schools of the basic medical sciences.

"However, three or four of the latter may well progress directly to four-year programs after they have become firmly established," the *Journal* said.

The four-year schools: The University of Arizona College of Medicine, Tucson; University of California, San Diego, School of Medicine; University of Connecticut School of Medicine, Farmington; Milton S. Hershey Center, Pennsylvania State University, Hershey; Mt. Sinai School of Medicine, New York City; South Texas Medical School, University of Texas, San Antonio; University of Massachusetts, and Toledo State College of Medicine, Toledo, Ohio.

The two-year schools: Brown University Program in Medical Science, Providence, Rhode Island; University of Hawaii Medical School, Honolulu; Michigan State University College of Human Medicine, East Lansing; Rutgers University Medical School, New Brunswick, New Jersey; University of California at Davis, and the University of New Mexico School of Medicine, Albuquerque.

The University of New Mexico accepted its first class in September 1964. As a developing two-year school, it becomes eligible for full accreditation when its first class nears the end of the sophomore year.

Rutgers expects to admit a small class in September 1966. Arizona, Brown, Hawaii, Hershey, Michigan State, and South Texas are planning to begin in 1967. All of the 14 schools should be in operation by 1969 or 1970.

---

### **From The Connecticut State Department Of Health**

Streptococcal sore throat infections reported by local directors of health in Connecticut totaled 937 cases during the week ending January 29, down from 1228 cases, the previous week, said Franklin M. Foote, M.D., Commissioner, Connecticut State Department of Health. The high level of reported cases appears to reflect substantial occurrence of the disease in broadly scattered areas, rather than in a few concentrated communities.

Reported measles cases remained few in number at 13, compared with 11 the week before. Chickenpox was 224, against 256, mumps, 246 against 286, and infectious mononucleosis 27 against 36.

Gonorrhea reports came to 67, up from 55, while syphilis moved up to 21 from 14.

# Connecticut Medicine

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Manuscripts should be typewritten, double-spaced on white paper 8½ x 11 inches with adequate margins on firm paper. The original copy, not the carbon copy should be submitted. Carbon copies or single spaced manuscripts will not be considered. Authority for approval of all contributions rests with the Editorial Board, and the Board reserves the right to edit any material submitted. Receipt of manuscripts will be acknowledged and unused manuscripts returned. The publishers accept no responsibility for opinions expressed by contributors.

## STYLE

The first page should list title, the author (or authors), degrees, and any institutional or other credits. Bibliographies should conform to the style of the Quarterly Cumulative Index published by the American Medical Association. This requires in the order given: Name of author, title of article, name of periodicals with volume, page, month—day of month if weekly—and year. Number should be limited to absolute minimum. References should be numbered consecutively in order in which they appear in the text.

## LENGTH OF ARTICLES

Ordinary articles should not exceed 3,000 words (approximately 3 printed pages). Under exceptional circumstances only will articles of more than 4,000 words be published.

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Illustrations should be numbered consecutively and indicated in the text. The number, indication of the top, and the author's name should be attached to the back of each illustration. Legend should be typed, numbered, and attached to each illustration. Photographs should be clear and distinct; drawings should be made in black ink (preferably India ink) on white paper. For half tones, glossy photographs should be submitted. CONNECTICUT MEDICINE will bear the cost of printing two cuts accompanying manuscripts submitted for publication. The cost of printing more than two cuts must be borne by the author.

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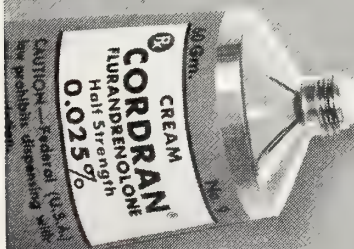
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# Connecticut Medicine

## editorials

### Medical Teaching Rounds

There is a general uneasiness both in minds of the public and also in the practicing physician, that future specialists in internal medicine will become mostly reliant on laboratory, computerized, non-personal techniques of management, and the patient as a human being with emotional and psychological aspects will be forgotten. If such physicians are to come into being, it must be due to the kind of training and environment to which they are exposed in their years in the medical school. A study by Payson and Barchas<sup>1</sup> on the nature of teaching rounds in three teaching and one university affiliated hospitals shows that there is a trend toward theoretical medicine and away from any emphasis on thorough patient care.

Rounds are rightly considered the most important formal teaching exercise of clinical discipline. Without doubt the senior man present usually sets and reinforces the model of such discipline at such rounds. It is here that the student and junior physician learn to observe the clinical performance of the leaders of American medicine. Rounds therefore may be expected to powerfully influence the orientation and performance of every new member of the profession.

A generation or more ago before laboratory and specialized techniques became a compelling aspect of medical practice, the senior physician and his group of juniors stood at the bedside. Here the senior questioned the patient to clarify his complaint, analyzed the meaning of the symptom to the patient and attempted to establish a few pertinent facts about the personality of the sufferer. He then

proceeded to make a searching physical examination, analyzing the true and false physical findings and often allowing the junior to elicit the physical findings under his direction. They then returned to the conference room where a list of alternative diagnoses were written down, each one considered in terms of the extensive physical findings and scanty laboratory data. Finally, two or three alternative diagnoses remained and the further work necessary to arrive at a final diagnosis was outlined.

Today Payson and Barchas find three different round groups. The house staff rounds spend over half their time with the patient. The regular attending physician in his rounds spends about one-fifth of his time with the patient. The special attending physician or senior spends about one-tenth of his time with the patient. The topic discussed also varied according to the rank of the senior physician. The time spent on discussion of physical factors in the patient's presence by the special attending physician was two per cent; by the regular attending physician, five per cent; and by the house staff 20 per cent.

No group spent more than 11 per cent of the time discussing factors other than physical, such as employment, social status, personal problems. The regular attending physician spent two per cent and the senior physician only 1.7 per cent on these "other" aspects. However, the time spent on discussing theory by regular attending staff was 26.5 per cent and by the senior attending 45.8 per cent. In short, there is a definite movement away from dealing with patients' personal problems and toward dealing with his physical problems and their

### THE COVER

#### LISTER INTRODUCES ANTISEPSIS

WHEN Surgeon Joseph Lister (1827-1912) of Glasgow Royal Infirmary removed dressings from James Greenlees' compound fracture, he found the wound had healed without infection—something unheard of before. For six weeks, beginning August 12, 1865, Lister had treated the boy's wound with carbolic acid. Now, Lister had proof of success of his principle of antiseptics—which was to revolutionize principles of wound care and to open new vistas in practice of surgery, of medicine, and of environmental sanitation. Hospitals were turned from houses of horror to houses of healing; countless lives were saved.

theoretical analysis, and the time so spent increased with the rank of the senior man. This startling finding suggests that pathophysiology, that is measurable by laboratory or physical techniques is taking time emphasis that would otherwise be given to interview and bedside examination.

It may be seen that on house staff rounds the proportion of time spent on personal factors was highest, but it was only eleven per cent of the time as compared to 48.3 per cent of the time spent on discussion of physical examination, laboratory data and theoretical analysis. Because of the limited time allotment for personal factors on regular and special attending rounds, the question may be asked whether students, internes, and residents are given an exemplary model for the handling of personal factors by the senior staff. These findings suggest that the teaching orientation of medical rounds in some outstanding teaching hospitals is not directed towards thorough patient care which requires careful study not only of the physical factors but also personal factors as well. The question of course arises whether spending time also on analyzing and understanding of personal factors are still necessary.

There is a prevalent belief that participants in medical rounds should learn about personal factors on other services and then form their own composite idea or model of comprehensive care. But for those who for one reason or another are unable to do this, the rounds as they are presently constituted will have an unfavorable influence on future clinical performance. It leads us to question whether future specialists in internal medicine will be able to carry out diagnostic and therapeutic programs involving the personal and other aspects of patient care besides the physical ones.

The way teaching rounds are presently constituted in university medical centers, the senior physicians seem to arrive at decisions by relating case findings to medical theory. They do not emphasize the physician's approach to the patient as a sick human being nor are they directed to the establishment of a doctor-patient relationship. The consequences of this performance would seem to imply that in the future the internist is likely to become mostly reliant on laboratory and non-personal techniques in the management of the sick person.

It isn't all black, however, as Dowling, et al. showed.<sup>2</sup> Teachers are appreciated for their knowledge of the subject, for their attitude towards the student, and for their skillful use of certain teaching techniques. The teacher demands of his student outside reading. He emphasizes basic pathophysiologic processes and exhibits knowledge of a specialty area within internal medicine. He can teach and

stimulate the graduating medical student to remain a student for life.

L.H.N.

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## Hepatojugular Reflux

If one compresses the abdomen with both hands gently and persistently for a minute to avoid pain, there is a reduced venous return from the venae cava inferior, thus dropping the pressure in it and its tributaries, mostly visible in the external jugular vein. The weight on the abdomen leads to thoracic breathing, replacing abdominal. Breathing is now in a more inspiratory position and this lowers intrathoracic pressure. Obviously a patient with severe emphysema who must use his diaphragm to ventilate, will resist intra-abdominal pressure thereby raising both intra-abdominal as well as intrathoracic pressure. The venous pressure will then reflect high intrathoracic pressure and will rise in the absence of heart failure.<sup>1,2,3</sup>

Hitzig<sup>4</sup> believed that abdominal compression forced extra blood into the heart and raised the venous pressure in heart failure. But the question could have been asked why the veins did not distend to accommodate for the increased volume in heart failure since normally the veins are very distensible. The answer of course came from Burch's studies<sup>5,6,7</sup> in which he showed that in heart failure there is a high venous tone which diminishes as heart failure improves. This increased venous tone seems to be a part of a neurogenic mechanism, since it subsides with sympathetic blockade. If there is an increased venous tone in heart failure, the explanation for the rise in venous pressure after abdominal compression follows logically. In normal patients the veins can relax to accommodate large volumes of blood without appreciable change in pressure. Patients in congestive heart failure have their venous system adjusted for a high tone which maintains a tight squeeze around the enclosed blood. Therefore, when pressure over the abdomen displaces blood from the splanchnic area, the displaced volume is forced into poorly distensible vessels thus raising the venous pressure. Apparently the venous pressure which in heart failure is high, can be brought to normal by a phlebotomy of 800 cc. In this case the abdominal compression test returns to normal.

The question of course is whether failure of the right ventricle itself raises venous pressure without





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You might also say that all interns aren't alike, either.





the aid of venous tone. This view is the basis of the "backward failure theory". Apparently failure of the right ventricle itself is not sufficient since Starr<sup>7</sup> destroyed the right ventricle in dogs without producing a rise in venous pressure. However, the pressure of the right ventricle is necessary to cause increased venous tone when it fails. It must therefore be the source of reflexes that cause increased venous tone and increased venous pressure. The increased venous tone associated with heart failure causes the blood that is displaced from the splanchnic area to move into a venous system that is tight. This raises the venous pressure throughout the venous system. The right ventricle cannot respond to the increased filling pressure caused by the displaced blood even if the pressure on the abdomen is kept elevated for one minute.

Certain precautions need to be exercised in order to obtain reliable results. The patient may involuntarily resist the pressure on the abdomen, therefore pressure must be gradual and he must be asked when any discomfort arises. The maximum pressure with minimum discomfort can be achieved by opening the hand widely or by using both hands to compress the abdomen. The patient should be asked to breathe with the mouth wide open, to avoid hyperventilation that itself may increase venous tone or to prevent a minor Valsalva maneuver. The effect on the column of blood in the jugular vein is observed only during inspiration to avoid the false rises during expiration, bronchospasm or minor Valsalva maneuvers. The compression on the abdomen is maintained for at least one minute to distinguish transient from persistent elevation. The pressure is best applied to the right upper quadrant, but if it is tender, then to other areas, even at the cost of less pronounced results.

Constant and Lippshutz have used this method on over five hundred patients.<sup>1</sup> They found that all patients with elevated venous pressure had a rise in jugular venous pressure of at least 1 cm. on abdominal compression. They found that many patients with normal venous pressures but with signs of congestive heart failure had an abnormal rise. Almost all patients with acute myocardial infarction showed an abnormal response to abdominal compression, even when other criteria of acute infarction were inconclusive. This test then helped to support the diagnosis. First they tested the effect of abdominal compression in jugular vein distention with the patient in the supine position. Then they propped up the patient to an angle of 45° and then measured the absolute level of venous pressure. The top level of normal is 4 cm. above the sternal border. They then applied abdominal compression and in one minute one can tell whether the venous pressure is in the normal range.

Thus abdominal compression test is an old one. It was first described by William A. Pasteur in 1885 and offered to the profession as a test of tricuspid regurgitation.<sup>2</sup> Rondot<sup>3</sup> soon realized the broader significance of this effect and considered that a positive response indicated weakness of the right ventricle and named it Hepatojugular reflux. He believed this term meaningful because if pressure was applied over a large congestive liver, much more jugular distension was produced than with pressure on a normal abdomen. He of course was not aware of the role of venous tone in its production, a development which came much later. Nor did he test patients with chronic lung disease with emphysema and asthma as Hitzig did in 1959 who found positive tests in them also.

The results of the test have been remarkably constant in the seventy-nine years since its introduction. The searching attempt to explain its dynamics has revealed much more than the value of its clinical usefulness. It has led to a synthesis of the old views of "backward failure" and new views of increased venous tone in heart failure. Understanding the dynamics of the hepatojugular reflux, will now lead to a more widespread and intelligent use as a routine part of every physical examination. The test will add but a minute to our routine examination of a patient, but it will tell us whether there is or is not clinical or subclinical heart failure. It will tell us whether there is advanced emphysema or asthma. But equally important, it will make us more acute clinicians, with better understanding of the positive role of venous tone in heart failure and other clinical conditions. It will probably make unnecessary manometric determination of venous pressure, therefore helping us to rely more on our physical examination and less on technical procedures.

L.H.N.

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## The LINC Takes A History

In spite of the homage devoted to the importance of the medical history, neither the method of history taking and recording nor the reliability and usefulness of the data collected has been studied as rigorously as the other tools of clinical medicine. This is due in large part to the fact that neither the method of history taking which varies widely from one physician to another, nor the data so assembled lend themselves well to research.

Traditionally the method of taking and recording medical histories involves several serious problems for both the practicing physician and the clinical research worker. History taking consumes a large amount of the physician's time with the result that inadequate histories frequently result from time limitation beyond his control. Then there is the laborious process of recording the findings in long hand. In consequence, histories are often not standardized, are incompletely and illegibly written. These characteristics greatly hamper information retrieval and hence the use to which the history data can be put in medical education, patient care, and clinical research.

There is therefore a drive on to improve methods of collecting and recording detailed clinical information directly from the patient. Most of them are self-administered systems designed to take standardized histories in a form which permits computer processing of patients' answers to given questions. The questionnaires consist of medical questions designed by clinical specialists to be answered "yes" or "no" by the patient without further qualification. Furthermore there are no alternative sets of questions to be asked in accordance with different patient responses. We know of course that the physician historian does vary the presentation of his questions depending in part on the responses of the patient. It is the flexibility of variation in questioning which enables the physician to take histories in great detail and which has been the fault of computer based history taking up to the present time.

Slack, et al.<sup>1</sup> have developed a computer based medical history system that is intended to introduce the flexibility in history taking which previous methods did not have. They used the LINC (laboratory instrument computer) for their pilot study which was limited to symptoms of allergy. It is a small general purpose high speed digital computer,

especially designed for the collection of data (on-line) directly by the computer and the processing of the data at least as fast as they are generated. The instrument has a typewriter keyboard for direct input to the processing unit and two magnetic tape units for both storage and retrieval. Finally there is a cathode-ray oscilloscope resembling a television screen which is capable of displaying easily readable statements.

The questions in the medical history system are presented to the patient who sits in front of the computer looking at the screen. They provide the patient with four possible responses; Yes, No, don't know and don't understand. Then the question presentation is varied in accordance with the patients' responses. Like the physician, the computer historian also diversifies. When the computer gets a "yes" response, it follows by a series of specific qualifying questions. A "no" response to a general question results in skipping of unnecessary qualifying questions and the presentation of another general question, just as an astute clinician would. When the answer to certain questions are don't know and the questions not understood, these questions are clarified and explained with varying and simplified terminology.

The patient is allowed to correct errors or change his mind by deleting the number he has pressed on the typewriter and he can then answer the question again. When he is satisfied with his response he presses a bar which enters the answer in the computer memory and a new question appears simultaneously on the screen. Magnetic-tape stores questions and explanatory statements. The print-out statements matched with responses deemed of clinical significance are also stored on magnetic tape. When the history has been concluded, all print-out statements associated with the patient's responses are read into the computer and printed on paper by a teletype machine for immediate clinical use. Those questions consistently not understood can be altered and items of importance not originally part of the system can be easily included. In this way both the wording of some of the questions and the logic of their presentation were revised during the course of this experiment finally leading to a highly consistent and highly logical system of questions.

The 50 subjects in the pilot study at the University of Wisconsin Hospitals were evaluated for diagnosis and treatment of problems of allergy. The results are listed by the researchers as follows: it took an average of 15-20 minutes for a patient to complete the answers. The results of the computer history as printed out by the teletype was then compared in each case with the allergy history as recorded in the hospital chart by the physician. It



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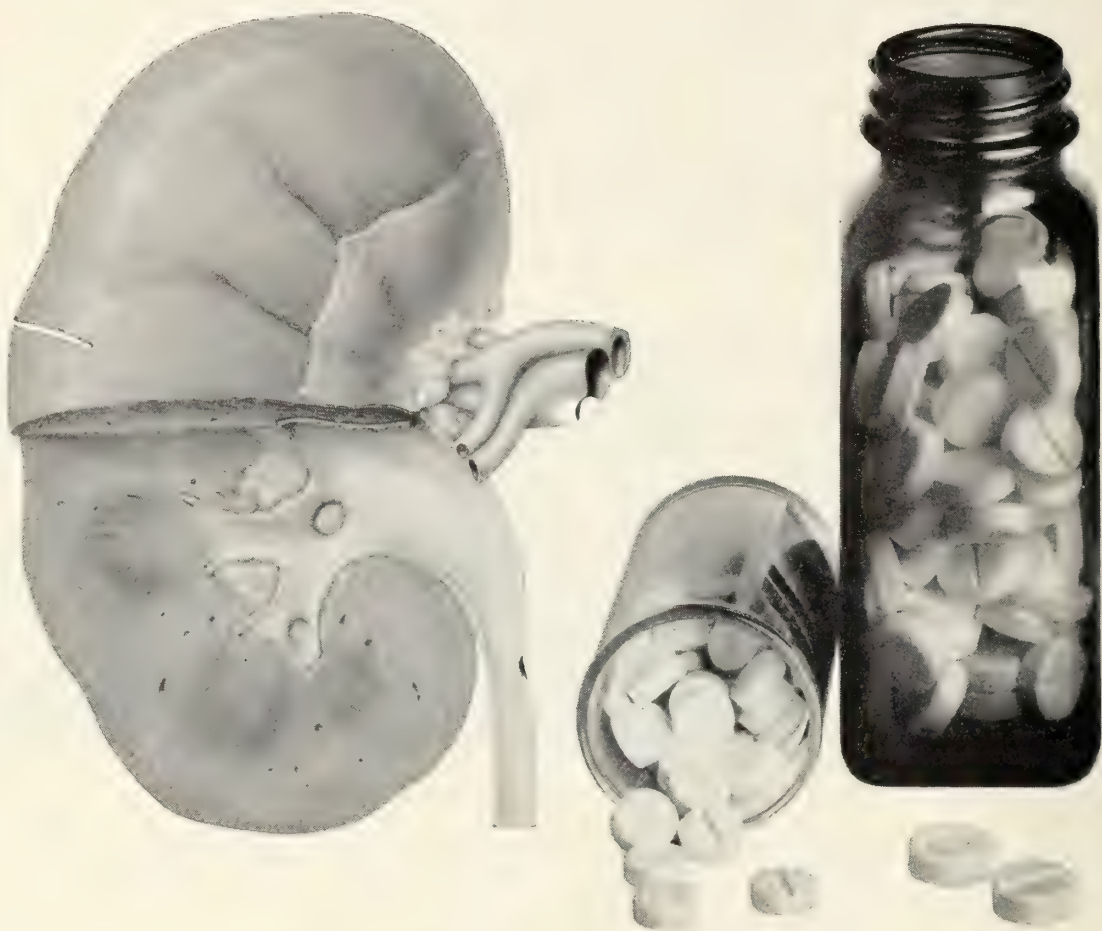
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precedes development

The development of chlorothiazide and probenecid were events of major importance, but perhaps even more important for the future was the Renal Research Program by which they were developed. When Merck Sharp & Dohme organized this program in 1943, it was expressing in action some of its basic beliefs about research:

- Many problems connected with renal structure and function were still undefined or unsolved. The Renal Research Program would begin its basic research in some of these problem areas.

- From knowledge thus acquired might come clues to the development of new therapeutic agents of significant value to the physician.

For example, the Renal Research Program put fifteen years into this search before chlorothiazide became available. But because these years had first led to a greater understanding of basic problems, the desired criteria for chlorothiazide existed before the drug was developed.

Along with other research teams at Merck Sharp & Dohme, the Renal Research Program continues to add new understanding of basic problems—understanding which will lead to important new therapeutic agents.

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turned out that the reliability of the computer as an asker of questions is great. A physician might get tired or not ask all the appropriate questions. The computer however is tireless, consistent, can take exactly repeated medical histories from the same patient. Inconsistencies are detected and studied in the patient's responses and the computer becomes an instrument also to test reliability and usefulness of various parts of the medical history. In fact the computer turned out to be superior to the physician recorded past histories. It was however less detailed when dealing with the present illness of asthma.

Without doubt the taking of a computer oriented history will be expanded from allergy to every branch of disease in time. The kinds of questions and the sequence will be worked out by clinical experts in each area and this will enrich the physician's ability to obtain a personal history when a computer is not available for the purpose.

What is of further interest is that the attitude of patients participating in the study was generally one of interest and approval. Twelve preferred the physician as historian, but 18 preferred the computer based system and 20 had no preference! That 38 out of the 50 should not have missed their personal physician is sufficient to lead us to serious thinking about the personal physician in our changing world. What we would like to know is how much was lost in the establishment of physician-patient rapport, since the computer was not programmed to obtain the data. Does this mean that in the university setting, the patients thought less about rapport than about receiving excellence in medical practice. It may be supposed that that is what the patients believed the computer was supposed to do.

What is certain however is that programming the computer by highly skilled clinicians in their respective specialties must produce questions which the physician can use in his own history taking thereby becoming a better physician more nearly approaching excellence in medical practice.

L.H.N.

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## Clues In Dealing With Cancer Patients

Cancer is the most feared of all diseases. It is looked upon as a killer. Both to the patient and the doctor it is a dreaded word. The patient is often aware of the fact he has cancer and is reacting to it whether he says so or not. He may not use

the word but all his verbal activity points to his clear understanding of the nature of the disease. Nothing he does or refrains from doing can alter it. This is strikingly different from heart disease which frequently can be stabilized through rest and medication. It is different from diabetes which the patient can control through diet and insulin. It is different in emotional disturbances when the person may learn through the therapeutic doctor-patient relationship to modify or eradicate conflicts which disturb his functioning.

The patient with cancer sees his disease as a purely medical one in which control of his physical or emotional activity cannot alter its progression. It is this fact more than any other which appears to influence his verbal and non-verbal activity especially in the advancing stage. Abrams, a social worker who sheds much light on this subject,<sup>1</sup> points out that the usual remark expressed by the patient before the diagnosis is confirmed is "I want to know the truth." However, his study suggests that this positive attitude fades or changes during subsequent stages of the disease.

In the initial stage there is direct truthful communication, faith in the physician, maintenance of good relations, no depression or hostility. Some patients even seem to acquire emotional strength, never previously observed. The patient knows the medical situation initially and the reasons for treatment. He follows advice faithfully. He is aware of the problem and is anxious for something to be done. He needs to talk, give details, when he first noted symptoms, why he delayed in seeking medical advice. Often he indicates the type of treatment he anticipates and fears. At this stage there is minimal need for defenses. He may even be optimistic. He wishes, he says "to know the truth."

One of the areas for caution at this stage, the study shows, is to guard against telling a patient more than he wants to know. One patient expressed this by saying "I was glad the doctor told me after removal of my breast that I had cancer, but I was frightened when he added that it had not spread—I never thought of *that*." Of course although one need not tell the whole truth, whatever one must say must be truthful. A distinguished scientist who after his operation knew the disease had spread said to a colleague "the surgeon told me he found a neoplasm which he believes he got completely—so if he thinks so, I'll agree." Obviously this patient was content with the partial truth.

In other words, at the time diagnosis is established and treatment recommended, communication is usually truthful if only partly so. The patient asks the doctor for information seeking further clarification from a significant professional or non-professional person in the setting. At this

stage it seems good for the patient to talk about cancer or tumor and speaking with physicians, with family and with some others too.

The interval after the initial treatment up to the advancing stage offers significant and unexpected clues to management. This "follow-up period" can cover a variable span, but as the time passes there is a distinct change in the patient's need to communicate. He retreats from talking about his diagnosis and offers unrealistic reasons for breaking appointments. We now must begin to decode his verbalization and behavior. We must understand he now has a need to escape from the clinic. He offers excuses for breaking appointments he must hurry home, he must not keep a friend waiting. The new attitude is retreating from the truth, and from significant other people in the setting with the exception of the physician.

Next comes the period of advancing disease, the one presenting the greatest problem for the patient, the doctor, the professional personnel and the family. For it is now apparent that the initial treatment has not eradicated the disease, that it has progressed. The patient knows this from pain in new areas and from the new treatments that are now recommended. Everyone is now anxious, unnerved and communication reaches an impasse. In this trying period the clue to optimism management is evident. The patients must now be given the opportunity to talk or not as they choose. Actually Abrams finds that the key is the difference between what the patient now asks as contrasted with earlier questions.

Physicians know that in this period the patients do not want to discuss their illness with them. The patients do not ask about their medical status. They employ excuses "the doctor was so busy," "he looked tired," "there were so many other patients to be seen," "I don't want to upset him because he has tried so hard to help me." The occasional patient who did inquire, Abrams states, usually indicated a wish not to have done so. This suggests that the patients really know the score but are sensitive about revealing their anxieties, especially to those best able to give them the answers and on whom they depend for treatment.

The patient in this stage becomes amnesic about the course of his illness, focuses on bodily symptoms or even suggests other possible explanations for their new found pain. There is a slow insidious change in the doctor-patient relationship. Patients fear abandonment and become more and more dependent upon the doctor. They show willingness to be referred to other physicians and limit their contact with paramedical personnel. They waited indefinitely without obvious impatience or resentment. They made no demands. Now they were concerned with diet, bodily symptoms. Should she take

Bufferin, a douche, walk more, bathe more, etc., all matters of daily living.

A patient who in the initial stage wanted to know the whole truth, now said "I've been wheezing at home, I'm tired all the time, I'm having trouble with my breathing—that's my greatest problem." Another patient said "if only my legs would improve I'd be all right." Now they are dissatisfied with everyone but the doctor. The patient departs with only one hope—that the physician will see him again. A return appointment is confirmation of hope that there is still some treatment to counter-act the disease. Now he relies upon the "omnipotence" of the medical profession.

The terminal stage begins when the disease is considered irreversible and treatment offered is only palliative. The dying patient is miserable, in pain, discomfort, and faces emotional problems of great magnitude, fear of death itself, fear of the ordeal of dying, and most devastating of all is fear of abandonment. For he becomes profoundly lonely, a state not reversed by drugs. The terminal stage Abrams describes as one in which there is suspended hopelessness; A patient who is sick enough to die knows it without being told. The patient continued control of self and the situation. Only a small percentage of patients in the terminal stage displayed reactions requiring special measures for control by the physician. Above all when there was respect for the patient as he was and wanted to be, there was a minimum of overt anxiety on the part of the patient and those concerned with his care.

A considerable number of patients in the terminal stage displayed a positive form of withdrawal or detachment. They developed a total acceptance of the nature and eventual result of the illness without any appearance of anxiety. They became detached from the realities of life, stopped talking about their children. At the same time they welcome the presence of a comforting figure who can meet the needs of helplessness.

The patients with marked depression were particularly disturbing to the doctor and their families. To overcome depression many focused their concern with a specific interest in their own posterity. One donated his cornea to the eye bank. He wished to leave behind a legacy.

Abrams suggests that religious faith can add comfort and support to many patients and should be considered in any program for optimum management, especially in the terminal stage. Furthermore, at this stage the patient also needs his doctor desperately and should not be abandoned. For the dying patient needs communication and exchange with those around him more desperately than do other types of patients. "Dying is lonely and closeness and warmth are the only remedies."





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It is clear that the patient with cancer changed his pattern of communication at different stages of the disease. These patterns in communication were the basis or clues for the doctor and paramedical personnel to consider in making total care more effective. The bedside clinician of past days knew these clues instinctively in his wise ministrations. Thanks to a gifted social worker these have been now made manifest to help all of us in dealing with cancer and perhaps other chronic relentless diseases.

L.H.N.

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## Active-Passive Tetanus Immunization

Tetanus in this country is no longer a serious problem except for the person who contracts it. Then the mortality is 50-100 per cent. The problem of prevention has been greatly improved with the administration of tetanus toxoid on a large scale. However, there remain large numbers of people who have not been immunized and who present themselves with cuts and abrasions, a potential source of tetanus. In these patients certain questions about the induction of passive-active immunity have as yet not been resolved. One is the amount of tetanus immune human globulin which is adequate for passive immunization. Another question is the relative merits of alum precipitated vs. fluid tetanus toxoid, in creating active immunity in such a patient. The final question is whether simultaneous inoculation of globulin and antigen will result not in creating active immunity but rather in mutual neutralization with the consequent vitiation of one or both activities.

If one reasoned that the smaller mobile toxoid molecule were given first and it would thereby have an advantage to become rapidly attached to antibody forming cells, initiate the antibody forming process and avoid mutual neutralization with the passively inoculated antibody, then a time interval between the injection of toxoid and antibody should work to promote active immunity. A corollary of this assumption would be that fluid toxoid should be superior to alum toxoid because of its greater mobility. Theoretically therefore fluid toxoid which is more mobile than alum toxoid

should be more efficient in creating active immunity in a patient at risk. So should an appropriate time interval which Levine, et al.<sup>1</sup> placed at three to four hours help to increase effect of the toxoid.

To answer these questions Levine, et al. designed experiments on 82 non-immune individuals to determine whether fluid or alum tetanus toxoid was the better agent in producing passive-active immunity and whether delayed or simultaneous administration of the passive antibody was the better schedule. Finally they wished to assess whether the dosage of 250 antitoxin units of human tetanus immune globulin was adequate or whether as Rubbo and Suri<sup>2</sup> claimed that 400 units were more efficient.

The duration of the delay between toxoid and globulin was dictated by two considerations. The first being that undue delay in the face of a tetanus-prone injury would be hazardous to the patient. The second one was that the delay must not exceed the possibility of encompassing a single office visit or outpatient visit because of the ever present risk that once a patient is dismissed he may not return. The experimental results were incorrect on both counts of the theoretical reasoning. Namely as regards the type of toxoid used as well as the reasoned schedule of inoculation.

The indicator of efficiency employed by Levine et al. was the serum-tetanus antitoxin titre of each subject sampled on the day of immunization, then on the one, two, three, seven, fourteen, twenty-one, twenty-eight, and fifty-sixth day after immunization. A secondary toxoid inoculation identical in dose and type of that given on the day of immunization was given on the twenty-eighth day.

The findings were as follows: Alum toxoid induced a thirty-fold higher secondary response than fluid toxoid; Simultaneous administration of human tetanus immune globulin did not preclude development of good active-immunity to alum toxoid, but the passive antibody was responsible for approximately a two week delay in the onset of active immunity. This emphasizes the importance of the dosage of immune globulin for this type of treatment. It suggests that there is an exceedingly narrow optimum, but that 250 antitoxin units is not far from optimum. Levine, et al. points out however that a larger dose such as suggested by Rubbo and Suri<sup>2</sup> might not be desirable since it could delay the period of the development of active immunity beyond the twenty-eighth day by partial suppression of the active response.

The conclusions to be drawn from these careful experiments, is first that theoretical considerations

may fall down when they are put to the experimental test. In this case there was no demonstrated contra-indication to the simultaneous administration of toxoid and globulin. Furthermore that alum toxoid is superior to fluid toxoid in establishing passive-active immunity in a patient at risk. Finally that 250 antitoxin units of globulin are near the maximum for induction of passive immunity.

L.H.N.

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## Antibodies In External Secretions

In a recent report Fischer, et al.<sup>1</sup> present results on antibodies in gastric juice and serum in four patients with pernicious anemia, in three patients with atrophic gastritis and "histamine-fast" achlohydria, all of whom had antibodies to the gastric parietal cells. For controls they studied five gastric juices from normal subjects. All were tested by the method of immunoelectrophoreses and immunofluorescence to identify the specific globulins in the serum and the gastric juice.

They were aware that there is a significantly higher incidence of circulating antibodies to a cytoplasmic microsomal component of the gastric parietal cell and the thyroid acinous cell in subjects with pernicious anemia or atrophic gastritis without pernicious anemia, than in normal subjects.

When tested by immunofluorescence, four out of the seven gastric juices obtained from patients with circulating parietal auto-antibodies gave evidence of positive antibody activity, two were equivocal, and one showed no antibodies. All the control gastric juices gave negative results. After careful analysis the authors found that the gastric parietal cell antibody in both serum and gastric juices is both of the IgG and IgA type, the former probably predominating.

The problem still remains whether the parietal cell antibodies are elaborated in the gastric mucosa or not since the two components are present in both gastric juice and serum. Synthesis in the gastric mucosa might be one explanation. In that case it would have to cross the mucosal barrier and enter the blood stream. Another explanation is that the antibody is formed in the lymph system and passes through the mucosal barrier into the gastric juice.

An alternative explanation is that some factors in the gastric mucosa determine that of the two antibodies, only the parietal cell antibody will pass across the gastric mucosa to enter the gastric lumen. We know that other circulating antibodies such as those to the cytoplasm of the thyroid acinar cell do not cross the mucosal barrier and do not appear in the gastric juice.

It has been suggested that a preferential secretion or local production in adjacent lymph nodes may account for some of the globulins present in fluids elaborated in different regions of the body. In the salivary gland there is probably local synthesis of IgA, a polymer which is found in saliva and colostrum but not in serum. In fact there is a growing body of evidence that in man immunoglobulins are normal components of various secretions such as tears, succus entericus as well as saliva and colostrum.

There is little doubt that nasal secretion also contains antibodies. The ease with which patients with normal nasal mucous membranes overcome nasal infection is well known. On the other hand, those patients unfortunate enough to have 'dry nose' with reduced nasal secretion suffer frequent and prolonged nasal infections with frequent sinus involvement.<sup>2</sup> These patients get worse with antihistamines and improve with cholinergic stimulation of nasal secretion.

The question of the nature of the immunoglobulins is important and has been subject to investigation now that techniques for identification of the globulins are available. In human saliva, colostrum, and lacrimal secretions, the predominant immunoglobulin is IgA whereas in serum IgG is the major gammaglobulin. In bile and in small intestinal secretions IgG predominates. Whether these are produced in response to the organisms to which these glands are subject is not yet established. Surely however the existence of these immune globulins in these secretions must present an important barrier to systemic infection.

We have then a new and important view of the antibodies found in various secretions. Some are elaborated in the gland which produces the secretion and serve a useful and therapeutic purpose. Others, however, are autoantibodies which in the case of pernicious anemia are either the result of the disease or the cause of the disease as is seen in the case of pernicious anemia and atrophic gastritis

L.H.N.

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*Taking an ECG?*

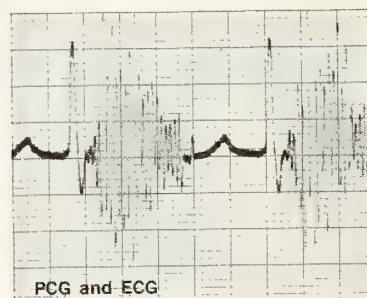
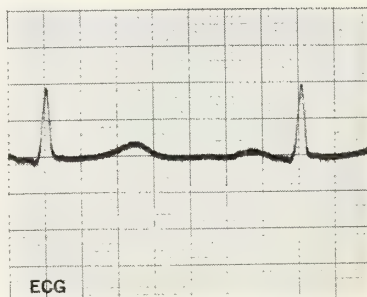
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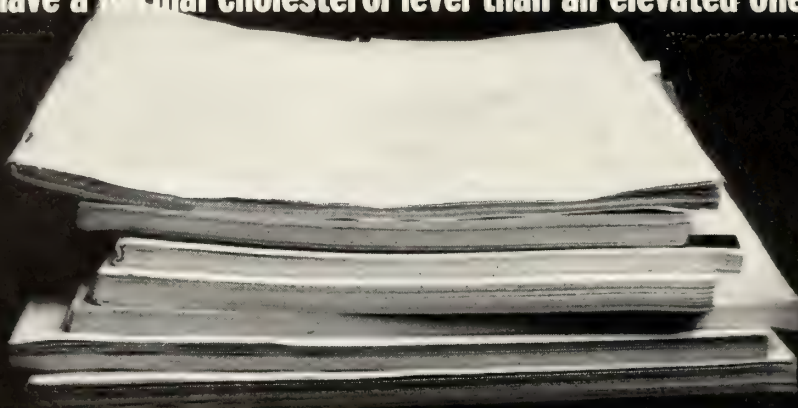
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# The Ponderal Index

There is increasing emphasis in American society on weight control because of justifiable concern about the effects of adiposity on health, function and longevity. This makes it imperative to take a hard look at the criteria by which we are going to judge overweight and the degree of overweight. We need to know when we are justified in designating a given patient as obese. Up to the present time the height-weight tables most commonly used as standards of overweight and obesity are those of the Metropolitan Life Insurance Company. Seltzer<sup>1,2</sup> points out that there are certain critical defects in these height-weight tables and that those using the tables of "desirable" weights for men and women should be aware of the severity and often unrealistic requirements of these tables and the marked extent to which they are below the known average weights of Americans, including young adults. But what method is an acceptable substitute, and how are we going to judge adiposity as distinct from overweight.

By definition overweight refers to the excess of body weight from a specific standard which as noted above is too severe. Obesity on the other hand refers to a condition of "fatness" or an excess amount of adipose tissue. If we look upon body weight as a result of the contribution of all the elements of body composition, bone, muscle, fat, tissue and fluid, then we can see that the excess weight in the overweight state does not specify whether it is the result of fat or other elements in the body, except in the very markedly overweight person. In short, not all overweight people are necessarily obese. This differentiation between overweight and obesity is very important so that we may recognize where the greater health hazards lie. We can do this if we could differentiate between the relative contribution of variances of the body compartments and "fatness".

Another element of confusion in the problem is the question of individual variations in the body build structure. There are ectomorphs, mesomorphs and endomorphs.<sup>3,4,5,6</sup> Some of these may have identical heights and weights although vary markedly in their adipose composition. The Metropolitan tables attempt to take into account body build through the use of the categories of small, medium and large frames, but these appear not to be based on actual measurements and no direction is offered for making such a distinction. Since overweight is correlated with increased mortality, it is justified to ask whether body build itself can in part be responsible for the association of underweight and overweight with mortality ratios.

Great strides have been made in the last decade in the field of body composition measurements for

we urgently need ways of judging the presence and extent of obesity as contrasted with overweight. One method has been skin-fold measurements.<sup>7</sup> For this a single skin-fold thickness measurement in the region of the triceps has been suggested. This however would require medical men to learn to use skin-fold calipers and tables to establish fatness in relation to these measurements.

Another method is the ponderal index which has come to be a most frequently used simple measure of body shape or build. This concept involves the transformation of the height and weight data in terms of the ponderal index—height (inches) over the cube root of weight (pounds). Seltzer's report<sup>2</sup> deals exclusively with the data of men based on the transposition of the weight for height categories into comparable ponderal indexes.

The ponderal index turned out to be a better index of linearity and laterality than simple broad height-weight categories. Furthermore it had the capacity of separating out body build types in the somatotype sense identifying dominant ectomorphs and dominant endomorphs and finding that obesity is the trademark of by far the largest proportion of the dominant endomorphs.

An analysis of the data for men of the Build and Blood Pressure Study 1959<sup>8</sup> on mortality ratio by means of the ponderal index demonstrated that there is not a straight line relation of increasing mortality with increasing weight for height as indicated by the insurance company figures. Instead there is a curvilinear exponential relation of mortality with linearity and laterality of body form. It is striking that there is no significant excess of actual mortality over that expected until the level of extreme laterality is reached. At this general level (over 30 lbs. overweight) the mortality ratio rises in a very steep, almost geometric, progression. The men with extreme laterality of body build are predominantly frankly obese.

It is important to the doctor to learn that below the level of extreme laterality the trend towards increased mortality is very modest. Stated another way the health risk of fat in the absence of frank obesity is therefore not clearly established. The analysis further demonstrates that physique or body build in the somatotype sense is an important factor in health and longevity and we must begin looking at our patients and attempt roughly to classify their somatotypes. Extreme ectomorphs appear to have the most favorable mortality experience whereas extreme endomorphs show substantial excess in mortality.

Seltzer emphasizes that the life insurance underweights are in all probability "normal" weight ectomorphs and not necessarily "slimmed-down" endomorphs or mesomorphs. It turns out that the

general use of such terms as "underweight" or "overweight" in connection with assessment of fatty tissue may have little relation to the persons actual fat status.

Studying the ponderal index, it becomes clear that body build type as well as obesity is associated with disease and mortality. This being the case, we must avoid the error of blaming on obesity what in fact is in part the effect of the body build type. There is little doubt that the body build type may also make people more prone to disease and this is particularly so in the frankly obese.

The ponderal index studies have opened up new avenues for investigation. We need to accumulate more descriptive body-build data including somatotype ratings as well as skin-fold thickness in connection with disease and mortality studies. In the meanwhile we must avoid oversimplifying the body build factor when it is so poorly characterized merely by height-weight categories. What we need now is conversion of the height-weight data into a ponderal index table which should be made available to all personnel working in the nutrition field.

The matter of desirable weights now needs revision in terms of definition, body-build, and the elements of body composition. However it must be recognized that a great deal of research is needed in this whole area if the ultimate goal of evaluating the useful potential of weight control as a public health measure is to be attained.

L.H.N.

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### A Preventable Cause Of Blindness: Temporal Arteritis

Regardless of how rare temporal arteritis is, when it occurs it ranks as a prime medical emergency

from the ocular standpoint. In no other disease does the prevention of blindness depend so much on prompt recognition and early treatment. As Shick<sup>1</sup> says "blindness is tragic, and preventable blindness is catastrophic." If the incidence of blindness from temporal arteritis is to be reduced, the physician must be thoroughly familiar with the syndrome, and remain alert to his important part in the diagnosis of the disease as well as its successful treatment, for it can be successfully treated.

Temporal arteritis has been known since 1890 when Hutchinson described the clinical picture. Now the clinical and histologic features of the disease have become widely known and appreciated. From the voluminous literature we are aware that the disease process can and often does involve arteries other than the temporals, especially those of the carotid system, although the predilection is for the temporal arteries and it is for this reason that the disease is rightly called temporal arteritis rather than what some have called cranial, granulomatous and giant cell arteritis.

The affected arteries are larger than normal, may be nodular and frequently appear to be solid cords with little or no lumen. This external change is caused by intimal proliferation with partial to complete occlusion of the lumen caused by inflammation of the media and adventitia with a granulomatous reaction with presence of foreign body giant cells. This causes pain and tenderness in the adjacent structures, such as scalp, face, eyes, temporo-mandibular joints. The reduced blood supply through these arteries may cause "intermittent claudication" of the muscles of mastication, and of course reduces blood supply to the optic nerve and retina leading to ischemic optic neuritis, ischemic retro-bulbar neuritis or occlusion of the central retinal artery. Visual loss may occur any time during the course of the disease but usually develops within the first few weeks.

Practically all reported cases have been over 55, most of them over 65. The disease may begin insidiously or sudden and the course is that of a sub-acute or chronic infection with local and systemic manifestations. The dominating and diagnostic symptoms and signs in addition to those mentioned above are severe headache, low grade fever and high erythrocyte sedimentation rate. In fact, the diagnosis is seriously in doubt if the E.S.R. is not significantly elevated. Accompanying these symptoms are other systemic reactions such as malaise, myalgias, arthralgias, anorexia and weight loss. These may precede the local symptoms and signs by a few weeks or months and persist for several weeks or months after the local signs have disappeared. Since the major complication is loss of vision in one or both eyes in approximately 50



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per cent of untreated patients, being alert to the disease will enable the physician to recognize it early enough and to institute treatment before the tragedy of blindness afflicts the patient.

Whenever an elderly patient over 60 complains of pain and tenderness in the temporal region with localized tenderness and induration, he should be carefully examined for tender indurated or pulseless temporal or occipital arteries and the symptoms should be evaluated from the viewpoint of possible temporal arteritis. If the E.S.R. is high and there is also a systemic reaction it raises high the index of suspicion. Rarely is a local biopsy indicated to confirm the suspicion. Generally the disease runs a self-limited course lasting 2-30 months (average 6 months). Relapses are uncommon, but once visual loss has occurred, this is permanent. The disease does carry a low but definite mortality risk, but generally it is benign and eventually, after a rather prolonged and often disabling illness, patients may expect to recover.

Shick<sup>1</sup> who has seen 17-18 patients a year at the Mayor Clinic describes their method of treating temporal arteritis. Their policy has been to treat as an emergency all the patients with this disease who are not completely blind. In the first two weeks, they administer by injection 200 mg. cortisone daily. If the patient has obtained the expected relief of symptoms and the E.S.R. has begun to return to normal, they change to oral administration of 50 mg. of cortisone four times daily for four more weeks. The dose is gradually reduced and administration is stopped in four to six weeks. Additional measures include a 2 mg. sodium diet and 3-6 grams potassium per day. They remind us that during and after the tapering off period of steroid therapy, most patients experience withdrawal symptoms and the E.S.R. rises but the reaction is transient and no resuming of dose is indicated.

Shick discusses the debatable value of anticoagulants. At the Mayo Clinic the anticoagulants are not used unless vision has been lost recently in one eye or ocular complications seem imminent as evidence by photophobia, transient blurring of vision or transient amlyopia. However once the effects of steroids has become evident then anticoagulants are discontinued. They also recommend intermittent inhalation of 100 per cent oxygen in some patients with recent visual impairment. Possibly an ischemic optic nerve or retina might be helped by such therapy especially if 5 per cent CO<sub>2</sub> were added to the O<sub>2</sub>.

Although the chief purpose of treatment with steroids is to suppress the arteritic process and so to safeguard any remaining vision, the symptomatic relief afforded by this treatment is striking. The

patients invariably feel much better, and the headache disappears or lessens within 48 hours after treatment is started, and the appetite and well being increases. This obvious improvement is received with grateful thanks by a pleased and relieved patient.

L.H.N.

#### Reference

1. Shick, R. M.: Temporal arteritis: Importance of early diagnosis and treatment. *The Heart Bulletin*, 14: 81, Sept.-Oct. 1965.

### More On Rapport: Examining The Patient's Feelings

A correct doctor-patient relationship is recognized as extremely important. To establish a rapport with the patient is to exhibit our understanding of the patient's suffering and communicating our sincerity to the patient so he can develop a trust in the physician.<sup>1,2</sup> The physician needs to bear in mind that the better to understand his patient, he must recognize that symptomatic and chance acts are not so entirely without meaning as is generally supposed. These things as Freud points out have a meaning and express impulses and purposes which are repressed and hidden from consciousness. To understand our patient we need to understand the dynamics of psychic life as expressed in acts, words, facial expressions. These are symptoms of a patient's feelings and can lead us to the discovery of many hidden events in the patient's psychic life.

Feelings then are symptoms of a patient's psychic life even as other symptoms are indicative of somatic activity. We are well schooled in the latter part of medical practice. Medical education is moving now in the direction of teaching how to examine a patient's feelings. Just as a physician does not become proficient in taking a good medical history and performing a good physical examination without expert teaching, so a physician requires correct teaching of appropriate interviewing techniques to be able to examine a patient's feelings. A physician does not become proficient in the use of these techniques solely through experience or by being naturally endowed with a sympathetic personality. These techniques must be taught.

It is only recently however that techniques to examine a patient's feelings have begun to evolve even though it is axiomatic that establishing a rapport between a patient and doctor is essential to success in the practice of medicine. In 1962 at the New York Medical College<sup>1</sup> a course was initiated for the purpose of teaching to all medical students interviewing techniques which they could use to obtain information about the emotional and mental

status of all patients. While this was done under the eyes of the Department of Psychiatry, these techniques once learned could be incorporated in the examination of all patients, not merely those with primary psychiatric difficulties, but also those with primary somatic illnesses.

The course is conducted by a psychiatrist with the assistance of a psychiatric social worker. The subjects are medical patients with psychiatric complications rather than primarily psychiatric patients. The interviews are conducted through a one way screen. At each session a student conducts the interview jointly with the psychiatrist while the remaining students and the social worker listen to the interview on the observation side of the screen. The student initiates and conducts the interview for the first half hour without interruption. During the second half hour the psychiatrist takes over the interview. On the observation side of the screen an instructor points out to the students the techniques as they are employed by the psychiatrist. There is here gathered much material for later discussion.

Privacy, adequate allotment of time, and an attitude of respect for the feelings if the patient are pointed out as essential. The student shakes hands with the patient after introducing himself. At this time he is advised to note the appearance and speech of the patient and above all to be aware of his own feelings. He is advised to approach the patient without prejudice and judgmental attitudes. He achieves empathy with the patient by expressing an understanding of the patient's difficulties and feelings. The interviews thus encourage the patient to talk further about himself. If the student is alert he will note the appearance, behavior and speech of the patient and will be able to verbalize for the patient many of his apparent but unexpressed feelings. Although the patient may deny such feelings, he usually develops an affinity with the doctor who can sense and accept conventionally unacceptable or irrational feelings.

The student is advised to ask open-end questions and when the patient requests direct advice, he is taught to turn the question back thereby urging the patient to consider possible answers of his own. Techniques for encouraging ventilation, giving reassurance and support and dealing with "blocking," silences, and weeping are described. The authors present an actual interview and how the emotional problem was resolved.

The patient was a 16 year old girl who entered several times in diabetic coma, because she refused to inject herself with insulin, stating she feared the needle. It turned out that in Puerto Rico her aunt

gave her the insulin, but in New York her mother refused, insisting she learn to become self-sufficient by taking the insulin herself. The student felt blocked. He was not able to elicit the patient's feelings about the quarrels with her mother. Instead he began to reiterate to the patient the dangers of not keeping up with the injections. Due to his own anxiety, he could not allow the patient to ventilate her feelings, but instead began to describe techniques of injection of the insulin which might reduce her fears. At this point the instructor intervened and expressed his understanding of the resentment the patient might be feeling towards her mother. This change succeeded and left the patient to elaborate on her resentment and the arguments she had had with her mother preceding each hospitalization. As she recounted her resentful feelings she recognized spontaneously that her inability to inject herself was related to her anger and resentment of her mother. She said "I must have been crazy at those times I didn't take the injections."

The errors here seem apparent. The resident tried to teach and not to explore the patient's feelings towards her mother. Both the medical resident and student experienced anxiety about examining the patient's feelings, and this anxiety prevented them from eliciting the necessary information for appropriate management. The student feared to disturb the patient emotionally and did not try to examine the patient's feelings. None of the questions he resorted to were aimed towards the patient's feelings. He was therefore unable to grasp in a concrete fashion how a patient's resentment and a physician's anxiety could block the way to gaining essential information.

Such direct observation of the failure of the medical student and the success of the instructor using clearly spelled out techniques have made possible the incorporation of these techniques into the student's own store of resources. The student at the beginning "was inclined to ask many questions to get the information right away." He "was afraid she was going to cry, so I changed the subject." He "didn't want her to be angry." He learned that some of the errors in the formation of rapport were due to his own anxiety. Some derived from insufficient knowledge of emotional problems. Some come from not considering his patient's feelings.

Apparently the course was a great success. The only criticism was that not all students can conduct interviews because of limitation of time. However, the great pressure of requests for more individualized instruction and personal supervision attest to the value the student body attached to this type of



## Blueprint for dealing with tension due to stress — Prolixin — once-a-day

For the patient who must be on the job mentally as well as physically, prescribe Prolixin. The prolonged tranquilizing action of as little as one or two mg. helps him cope with tension all day long. Markedly low in toxicity and virtually free from usual sedative effects, Prolixin is effective in controlling both anxiety associated with somatic disorders and anxiety due to environmental or emotional stress. Patient acceptance is good — because Prolixin is low in cost, low in dosage and low in sedative activity. Prescribe Prolixin.

**Side Effects, Precautions, Contraindications:** As used for anxiety and tension, side effects are unlikely. Reversible extrapyramidal reactions may develop occasionally. In higher doses for psychotic disorders, patients may experience excessive drowsiness, visual blurring, dizziness, insomnia (rare), allergic skin reactions, nausea, anorexia, salivation, edema, perspiration, dry mouth, polyuria, hypotension. Jaundice has been exceedingly rare. Photosensitivity has not been reported. Blood dyscrasias occur with phenothiazines; routine blood counts are recommended. If symptoms of upper respiratory infection occur, discontinue the drug and institute appropriate treatment. Do not use epinephrine for hypotension which may appear in patients on large doses undergoing surgery. Effects of atropine may be potentiated. Do not use with high doses of hypnotics or in patients with subcortical brain damage. Use cautiously in convulsive disorders. **Available:** 1 mg. tablets. Bottles of 50 and 500. For full information, see Product Brief.

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instruction. The technique is bound to spread and involve the practicing physician as well.

L.H.N.

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2. Nahum, L. H. The formation of rapport. *Conn. Med.*, 29: 10, 1965.
3. Gold, L. and Wolf, I. M.: Teaching psychiatric interviewing to medical students. *J.A.M.A.*, 194: 1014, Nov. 29, 1965.

## Digitalis And The Non-Failing Heart

Digitalis and its glycosides have been the mainstay of the treatment of congestive cardiac failure since William Withering adapted the foxglove formula of the "old woman of Shropshire" in the mid-eighteenth century. To this day, however, the mechanisms of action of these agents remain obscure. In recent years many studies of their effects at the cellular level have been done, and much information is available about ion transfer, myocardial metabolism, and contractile proteins. Page<sup>1</sup> summarizes a good deal of this information and points out that cardiac glycosides inhibit the active transfer of sodium ions out of heart muscle cells at the external surface of the cell membrane. This process seems to involve a displacement of potassium ions from a critical site at this surface. Thus there is a net cellular accumulation of sodium, and, secondarily, accumulation of chloride, loss of potassium, and fall in the potential difference across the resting cell membrane. The relation of these and similar observations to the therapeutic action of digitalis preparations, however, remains unclear.

It is generally accepted that the beneficial effects produced by digitalis administration in congestive heart failure result from a direct stimulation of myocardial contraction, and thereby an augmentation of cardiac output and lowering of ventricular end-diastolic pressure. There is considerable confusion about the effects of digitalis on the non-failing heart, however, and Braunwald, Mason, and Ross<sup>2</sup> have recently presented new and illuminating data bearing on this question.

Contractile force was measured directly in a group of patients not in failure and on cardiopulmonary bypass, by means of a strain gauge arch type of force transducer. In all instances, the contractile force of both right and left ventricular muscle segments was significantly increased after the injection of digitalis glycosides. The authors point out, however, the limited applicability of these observations to intact hearts because of anesthesia and surgical exposure. Consequently, studies of the rate of rise

of intraventricular pressure during isometric contraction were carried out in conscious subjects with non-failing hearts, utilizing a catheter with a high-fidelity micromanometer at its tip. Again, in all instances, the peak rate of change was significantly elevated after digitalization. In some instances a small presystolic elevation also took place, suggesting that the drug also stimulated the force of atrial contraction. In a series of patients with enlarged hearts but not in failure, digitalization reduced the absolute oxygen debt after exercise.

In another study rats were subjected to aortic constriction, and observations made on the development of left ventricular hypertrophy in groups which received no medication, and daily doses of digitalis. In the non-digitalized group, the average ventricular weight was 18 per cent greater than that of controls at the end of 30 days of constriction. In the digitalized group the difference was 9 per cent. In addition, the mortality from heart failure was significantly lower in the digitalized group.

It would appear that digitalis is capable of improving the contractile force of the normal-sized and the enlarged non-failing heart. Although in the minds of many clinicians overt failure and certain arrhythmias are the only indications for the use of digitalis, these studies would seem to offer a rational basis for more liberal use. Braunwald suggests that the administration of digitalis to patients with heart disease but not in heart failure may be indicated, particularly in situations where an excessive hemodynamic burden is anticipated, such as major surgery, parturition, etc. Routine digitalization prior to operations on the heart is carried out in many centers, and although no controlled data is available, it is felt that this precaution improves the course of such patients.

H.L.

### References

1. Page, E.: The actions of cardiac glycosides on heart muscle cells. *Circulation*, 30: 237, 1964.
2. Braunwald, E., Mason, D. T., and Ross, J.: Studies on the cardiocirculatory actions of digitalis. *Medicine*, 44: 233, 1965.

### Need a New Auto Emblem?

A supply of auto emblems, bearing the insignia of The Connecticut State Medical Society, is kept on hand at all times at the headquarters offices at 160 St. Ronan Street, New Haven, Connecticut. The price of each emblem is \$5.00 postpaid.

# Keranil ointment for psoriasis

## "a substitute for chrysarobin"

A frequent question at medical meetings is, "What is new for psoriasis?". This advertisement brings you a new product for this disease. It is Keranil ointment and has as its active ingredient chloranil, known also as tetrachloro p-benzoquinone.

Teichmann and Horvath studying polyoxyethylene formulations of chloranil made the following observations:

### SUMMARY OF CLINICAL RESULTS WITH CHLORANIL

| Concentration | Total<br>Number of<br>Cases | Much<br>Improved** | Improved* | Unimproved | Aggravated |
|---------------|-----------------------------|--------------------|-----------|------------|------------|
| 10%           | 63                          | 39                 | 14        | 6          | 4          |
| 5%            | 30                          | 16                 | 10        | 4          | 0          |

\*\* Denotes resolution of at least 50%.

\* Denotes resolution up to 50%.

### DURATION OF TREATMENT

| Number of Cases             | 14     | 24    | 18     | 14     | 9      | 3      | 7      | 4      |
|-----------------------------|--------|-------|--------|--------|--------|--------|--------|--------|
| Duration (weeks and months) | 2 wks. | 1 mo. | 2 mos. | 3 mos. | 4 mos. | 5 mos. | 6 mos. | 8 mos. |

The types of psoriasis included (parentheses indicate number of cases); Generalized (31), Palms and soles (7), Legs and feet (18), Scalp and ears (27), Groin (3), Neck (5) and Vulva (2).

Keranil Ointment appears to be most effective against the typical psoriatic plaque characterized by heavy scales. Furthermore, it appears to benefit both palmar and plantar plaques as well as intertriginous lesions and to be least effective against the small guttate lesions.

*Precautions:* Irritations are manifest as a suppurative follicular involvement accompanied by an erythema and as a lymph adenopathy in the drainage area of the inflammation. These irritations subside on withdrawal of the drug. Sensitization has been encountered. Keranil ointment is discoloring to skin and to clothing.

*Availability:* Keranil ointment is available in one ounce jars as a 10% concentration of choranil in a polyoxyethylene carrier.

#### References:

Teichmann, W. O. and Horvath, P. N.: Southern Medical Journal 50, 1521 (1957).

*Literature and samples on request.*

# Salem Pharmacal

Naugatuck, Connecticut



174th ANNUAL MEETING  
of the  
CONNECTICUT STATE MEDICAL SOCIETY

Statler-Hilton Hotel  
10 Ford Street, Hartford, Connecticut

April 26, 27, 28, 1966

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PROGRAM COMMITTEE



PAUL F. McALENNEY

PAUL F. McALENNEY, *New Haven, Chairman*

RUDOLF E. KLARE, *Woodstock*

DAVID BABBOTT, *Hartford*

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MESSAGE FROM THE PRESIDENT

Once again the Connecticut State Medical Society convenes on April 26, 27, 28th to conduct its 174th Annual Meeting. As has been the custom in the past, major effort has been engaged in to make both the scientific and business sessions better than ever. The administrative personnel and program committee have put together enough business and scientific data to keep us busy during these three days.

It will be well worth while for all of us to plan to spend these three days in Hartford at the Statler Hilton Hotel and enjoy the sessions and reunions with our colleagues who will be present from throughout the state.

JAMES R. CULLEN

## GENERAL INFORMATION

### Read Carefully

#### REGISTRATION:

The registration desk will be located on the mezzanine floor and everyone attending the meeting is requested to register. There will be no charge for registration and all members of the Society will be given a guest luncheon ticket when and only if they register.

#### PARKING:

There are ample parking facilities at the hotel and in the surrounding area. If you wish, you may drive up to the door of the hotel and an attendant will park your car for you.

#### TELEPHONE:

Telephone messages will be received at Hartford 249-5611.

#### LUNCHEONS:

Luncheons will be served in the City Rooms on the Mezzanine on April 27 and 28 and ALL MEMBERS OF THE SOCIETY REGISTERING WILL BE THE GUESTS OF THE SOCIETY. PLEASE REMEMBER, A LUNCHEON TICKET WILL BE GIVEN TO MEMBERS ONLY IF THEY REGISTER.

#### HOTEL ACCOMMODATIONS:

Persons who wish to remain overnight should make reservations not later than two weeks prior to opening date of the meeting. Reservations will be held until 6:00 P.M. on the day of arrival unless later hour is specified. Please indicate in your letter that you are attending the Connecticut State Medical Society Meeting. Your letter should be directed to the Front Office Manager, Statler-Hilton Hotel, 10 Ford Street, Hartford 06103, Connecticut. Special reservation cards are available in the Society office and will be mailed to members upon request.

#### ANNUAL DINNER:

The Annual Dinner will be held at the hotel on Wednesday, April 27, 1966. The social hour will be at 6:15 P.M. and the dinner at 7:00 P.M. All persons attending the dinner will be the guests of the Society at the social hour which will begin *promptly* at 6:15 P.M. and end *promptly* at 7:00 P.M. Your reservation for dinner should be sent in as soon as possible.

#### PROGRAM:

General scientific sessions will be held in the terrace room from 9:30 A.M. to 3:30 P.M. Section meetings will begin at 3:30 P.M. and will be held in the rooms listed in the program.

#### EXHIBITS:

The technical exhibits will be located in the ballroom. Physicians should take advantage of the opportunity to review "under one roof" what is new and timely in the goods and services available to the Connecticut physician.

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## PROGRAM

Tuesday, April 26

MEZZANINE

### Annual Meeting of the House of Delegates

KENNETH F. BRANDON, *Hartford, Speaker of the House, presiding*

10:00 CALL TO ORDER

BUSINESS SESSION

1:00 LUNCHEON FOR OFFICERS, MEMBERS OF THE HOUSE AND GUESTS

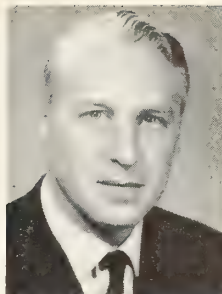
2:00 RESUMPTION OF BUSINESS

Social hour immediately following the adjournment of the meeting.





FENTON SCHAFFNER  
New York City



W. H. J. SUMMERSKILL  
Rochester, Minnesota



LOUIS R. WASSERMAN  
New York City

## Wednesday, April 27

9:00 REGISTRATION—MEZZANINE

### TERRACE ROOM

9:30 CALL TO ORDER—Orvan W. Hess, *New Haven, President of the Society*  
Address of Welcome—Charles E. Jacobson, Jr., *Manchester, President, Hartford County Medical Association*

PAUL F. McALENNEY, *New Haven, presiding*

9:45 DRUG INDUCED HEPATIC INJURY

FENTON SCHAFFNER, *New York City; Associate Professor of Pathology and Medicine, Columbia University College of Physicians and Surgeons; Head of Liver Group, Department of Medicine, Mt. Sinai Hospital*

10:30 HEPATIC DISEASE—SOME RECENT ADVANCES IN TREATMENT

WILLIAM H. J. SUMMERSKILL, *Rochester, Minnesota; Consultant in Medicine and Director, Gastrointestinal Unit, Mayo Clinic*

11:10 INTERMISSION TO VISIT TECHNICAL EXHIBITS

11:40 POLYCYTHEMIA

LOUIS R. WASSERMAN, *New York City; Director, Department of Hematology, Mt. Sinai Hospital; Associate Clinical Professor of Medicine, Columbia University College of Physicians and Surgeons*

12:20 POST TRAUMATIC EPILEPSY

A. EARL WALKER, *Baltimore, Maryland; Professor of Neurological Surgery, Johns Hopkins University School of Medicine; Neurosurgeon-in-charge, Johns Hopkins Hospital*

1:00 LUNCHEON—CITY ROOMS

INTERMISSION TO VISIT TECHNICAL EXHIBITS

DAVID BABBOTT, *Hartford, presiding*

2:00 DISORDERS OF CORTISOL PRODUCTION

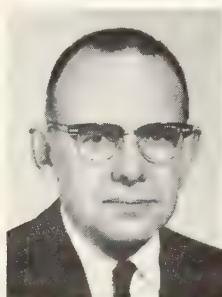
FRANK H. TYLER, *Salt Lake City, Utah; Professor of Medicine, University of Utah College of Medicine*

2:40 THE BATTERED CHILD WITH INNOCENT PARENTS

JOHN CAFFEY, *Pittsburgh, Pennsylvania; Visiting Professor of Pediatrics and Radiology, University of Pittsburgh School of Medicine; Radiologist, Children's Hospital, Pittsburgh*



A. EARL WALKER  
Baltimore, Maryland



FRANK H. TYLER  
Salt Lake City



JOHN CAFFEY  
Pittsburgh, Pa.

Wednesday, April 27

## MEETINGS OF SECTIONS OF THE SOCIETY AND GUEST ORGANIZATIONS

### WOMAN'S AUXILIARY TO THE CONNECTICUT STATE MEDICAL SOCIETY

22ND ANNUAL MEETING

CORNER HOUSE, FARMINGTON

President: Mrs. Williams R. Richards, *New Haven*

Recording Secretary: Mrs. Nicholas E. Creaturo, *Fairfield*

Corresponding Secretary: Mrs. Anthony P. Cipriano, *New Haven*

10:00 REGISTRATION

10:30 BUSINESS MEETING

Guest Speaker: FRANCIS GALLO, *Chairman*

*Board of Directors of COMPAC*

1:00 LUNCHEON

Guest Speaker: MRS. ASHER YAGUDA, *President-Elect*

*Woman's Auxiliary to the American Medical Association*

### SECTION ON DERMATOLOGY

3:30

Room 424

President: Patrick N. Brown, *Meriden*

Secretary: Saul Rosenberg, *Bridgeport*

### CURRENT CONCEPTS OF COLLAGEN DISEASE

LOUIS FERNANDEZ-HERLIHY, *Boston; Clinical Fellow, Lahey Clinic*

### JOINT MEETING

#### SECTION ON GASTROENTEROLOGY

President: Howard M. Spiro, *New Haven*

Secretary: Saul S. Milles, *Hamden*

#### SECTION ON INTERNAL MEDICINE

President: William E. Swift, Jr., *New Haven*

Secretary: Robert J. Molloy, *Hartford*

3:30

Rooms 416-420

### DISCUSSION OF A PATIENT WITH LIVER DISEASE

Moderator: ROBERT L. SCHEIG, *New Haven Assistant Professor of Medicine, Yale University School of Medicine*

Panel: WILLIAM H. J. SUMMERSKILL, *Rochester, Minnesota, Consultant in Medicine and Director, Gastrointestinal Unit, Mayo Clinic*

FENTON SCHAFFNER, *New York City; Associate Professor of Pathology and Medicine, Columbia University College of Physicians and Surgeons; Head of Liver Group, Department of Medicine, Mt. Sinai Hospital*

### JOINT MEETING

#### SECTION ON NEUROSURGERY

President: Franklin Robinson, *New Haven*

Secretary: Robert H. Sturman, *Waterbury*

#### SECTION ON NEUROLOGY

President: Bernhard A. Rogowski, *New Haven*

Secretary: John C. Moench, *New Haven*

3:30

Room 408

### NEOPLASIA AND THE CENTRAL NERVOUS SYSTEM

ELIAS E. MANUELIDIS, *New Haven; Professor of Pathology, Yale University School of Medicine*



Wednesday, April 27

SECTION ON OBSTETRICS AND GYNECOLOGY

3:30 Washington Room

President: Charles B. Cheney, *New Haven*

Secretary: G. Lawrence Austin, Jr., *Hartford*

THE TIRED MOTHER'S SYNDROME

LEONARD L. LOVSHIN, *Cleveland, Ohio; Department of Internal Medicine, Cleveland Clinic*

SECTION ON PATHOLOGY

3:30 Room 436

President: Richard D. Otis, *Hartford*

Secretary: Peter B. Hukill, *New Haven*

ARTIFICIAL HEART RESEARCH—CURRENT STATUS

BERT K. KUSSEROW, *Burlington, Vermont; President, American Society for Artificial Internal Organs, Associate Professor, Department of Pathology, University of Vermont College of Medicine*

SECTION ON PEDIATRICS

(Hezekiah Beardsley Club)

3:30 Room 440

President: James H. Root, Jr., *Waterbury*

Secretary: Paul Teiger, *Waterbury*

INFECTIONS IN PEDIATRICS

BURTIS B. BREESE, *Rochester, New York; Clinical Professor of Pediatrics, University of Rochester School of Medicine*

SECTION ON PHYSICAL MEDICINE

3:30 Room 412

President: Robcliff V. Jones, Jr., *New Haven*

Secretary: Sanford Harvey, *Middletown*

NEW TECHNIQUES IN SPLINTING

CARL V. GRANGER, *New Haven; Assistant Professor of Physical Medicine, Yale University School of Medicine*

SECTION ON PREVENTIVE MEDICINE AND PUBLIC HEALTH

3:30 Buffalo Room

Chairman and Secretary: J. Howard Johnston, *Wethersfield*

TRANSMISSION OF ELECTROCARDIOGRAMS FROM A COMMUNITY HOSPITAL FOR REMOTE COMPUTER ANALYSIS

ROBERT J. DOBROW, *Hartford; Senior Resident in Medicine, Hartford Hospital*

SECTION ON PROCTOLOGY

3:30 Boston Room

President: Bernard J. Kaplan, *Hartford*

Secretary: Sanford Savin, *Bridgeport*

PEDIATRIC PROBLEMS IN PROCTOLOGY

RICHARD M. ALEXANDER, *Great Neck, New York; Chief Proctologist, Long Island Doctor's Hospital, Roslyn, New York*

SECTION ON UROLOGY

3:30 New York Room

President: Harold A. Lear, *Hartford*

Secretary: Robert H. Hepburn, *Hartford*

RENAL TUBULAR DISORDERS IN CLINICAL MEDICINE

MICHAEL Z. LAZOR, *Hartford; Internist*

Wednesday, April 27

CONNECTICUT DIABETES ASSOCIATION

3:30

Room 404

President: William G. Leeds, *West Hartford*

Secretary: James C. Hart, *New Haven*

DRUG MANAGEMENT OF THE ORGANIC HYPOGLYCEMIC

MARTIN G. GOLDNER, *Brooklyn, New York*; Professor of Medicine, State University of New York; Director, Department of Medicine, Jewish Hospital of Brooklyn, New York

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ANNUAL DINNER OF THE SOCIETY

STATLER-HILTON HOTEL

10 Ford Street

Hartford, Connecticut

Social Hour 6:15 P.M.

Dinner 7:00 P.M.

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PROGRAM

INTRODUCTION OF NEWLY ELECTED OFFICERS — STEVENS J. MARTIN, *Hartford, Chairman of the Council*

ORVAN W. HESS, *New Haven, President, presiding*

PRESENTATION OF GUESTS AND DELEGATES FROM STATE MEDICAL SOCIETIES

FIFTY YEAR MEMBERSHIP AWARDS

Daniel Thomas Banks, Bridgeport

Genesis Frank Carelli, New Haven

James Lowry Gilday, Bridgeport

Daniel Patrick Griffin, Bridgeport

Isao Hirata, Sr., New Haven

Anthony Joseph Mendillo, New Haven

James Raglan Miller, West Hartford

Raymond Vincent Quinlan, Meriden

Harry Stephen Reynolds, Ellington

Upton Sharets Reich, Trumbull

Frank Forester Simonton, Enfield

Anthony Paul Vastola, Waterbury

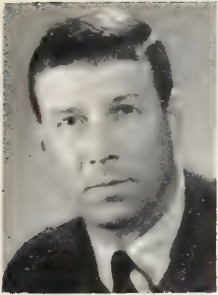
*Guest Speaker*



DURWARD G. HALL, M.D.

*The Honorable Durward G. Hall, Member of Congress, U. S. Representative from Missouri;  
Delegate to the American Medical Association; Practicing Surgeon*





EDWARD B. HAGER  
*Boston, Massachusetts*



RICHARD E. WILSON  
*Boston, Massachusetts*



WILLIAM B. SCHWARTZ  
*Boston, Massachusetts*



MILTON HELPERN  
*New York City*

## Thursday, April 28

9:00 REGISTRATION—MEZZANINE

### TERRACE ROOM

9:05 FILM—*"The One Who Heals"* Produced by Department of Medicine and Religion, AMA

RUDOLF E. KLARE, *Woodstock, presiding*

9:45 ORGAN TRANSPLANTS—MEDICAL MANAGEMENT

EDWARD B. HAGER, *Boston Massachusetts; Instructor, Harvard Medical School; Associate in Medicine, Peter Bent Brigham Hospital; Assistant Director, Cardiorenal Laboratory, Peter Bent Brigham Hospital*

10:30 ORGAN TRANSPLANTS—SURGICAL MANAGEMENT

RICHARD E. WILSON, *Boston Massachusetts; Associate in Surgery, Harvard Medical School; Associate in Surgery, Peter Bent Brigham Hospital*

11:10 INTERMISSION TO VISIT TECHNICAL EXHIBITS

11:40 THE USE OF DIURETICS

WILLIAM B. SCHWARTZ, *Boston, Massachusetts; Professor of Medicine, Tufts University School of Medicine; Senior Physician and Chief, Renal Service, New England Medical Center Hospitals*

12:20 OFFICIAL INVESTIGATION OF SUDDEN SUSPICIOUS AND VIOLENT DEATH—WHAT IS NEEDED

MILTON HELPERN, *New York City; Professor and Chairman, Department of Forensic Medicine, New York University Schools of Medicine; Consultant Pathologist, Bellevue Hospital; Chief Medical Examiner, New York City*

(Program arranged with Association of Medical Examiners of Connecticut)

1:00 LUNCHEON—CITY ROOMS

INTERMISSION TO VISIT TECHNICAL EXHIBITS

## PROGRAM ARRANGED WITH THE CONNECTICUT SOCIETY OF AMERICAN BOARD SURGEONS AND THE SECTION ON ORTHOPEDICS

2:00-3:30 A SYMPOSIUM ON TRAUMA

Moderator: WILLIAM W. L. GLENN, *New Haven; Professor of Surgery, Yale University School of Medicine*

Panel: RONALD A. MALT, *Boston, Massachusetts; Surgical Services, Massachusetts General Hospital; Department of Surgery, Harvard Medical School*

F. A. SIMEONE, *Cleveland, Ohio; Professor of Surgery, Western Reserve University School of Medicine; Director of Surgery, Cleveland Metropolitan General Hospital*

JOHN D. STATES, *Rochester, New York; Clinical Instructor, Division of Orthopedic Surgery, University of Rochester School of Medicine; Associate Attending Surgeon, Strong Memorial Hospital and Rochester General Hospital*



RONALD A. MALT  
*Boston, Massachusetts*



F. A. SIMEONE  
*Cleveland, Ohio*



JOHN D. STATES  
*Rochester, New York*

Thursday, April 28

## MEETINGS OF SECTIONS OF THE SOCIETY AND GUEST ORGANIZATIONS

### SECTION ON ALLERGY

3:30 Room 408

President: Eugene H. Walzer, *Bridgeport*

Secretary: A. Arthur Fierberg, *Hartford*

CURRENT KNOWLEDGE AND PRACTICES IN THE DIAGNOSIS AND TREATMENT OF ALLERGIC REACTIONS TO INSECT STINGS

HARRY LOUIS MUELLER, *Boston*; Chief, Division of Allergy, *The Children's Hospital Medical Center*

### SECTION ON ANESTHESIA

3:30 Room 424

President: Pierino D'Elia, *New Haven*

Secretary: James B. Given, *Hartford*

ELECTRON TRANSFER—IS THIS THE LESION IN SHOCK?

WILLIAM S. HOWLAND, *New York City*; Chairman, Department of Anesthesiology, *Memorial and Sloan-Kettering Cancer Institute*

### SECTION ON GENERAL PRACTICE

3:30 Room 404

This will be an organizational meeting with election of officers and developing of plans.

### SECTION ON OPHTHALMOLOGY

President: Charles T. Schechtman, *New Britain*

Secretary: William B. Brewster, Jr., *Hartford*

3:30 BUSINESS MEETING—Room 416

6:00 SOCIAL HOUR—Room 412

7:00 DINNER—Rooms 416-420

8:15 Guest Speaker: CHARLES M. BARBOUR, *Hartford*; *Anesthesia Department Hartford Hospital*:  
Title: IT CAN HAPPEN TO YOU—ACUTE MEDICAL AND ANESTHETIC EMERGENCIES — MEDICO-LEGAL ASPECTS AND TREATMENT



Thursday, April 28

SECTION ON ORTHOPEDICS

President: Robert P. Fornshell, *Danbury*

Secretary: Charles T. Flynn, Jr., *Meriden*

2:00-3:30 Terrace Room—Joint Meeting with Connecticut Society of American Board Surgeons—(See General Program—Thursday, 2:00 P.M.)

Following the clinical session, the Section on Orthopedics will hold a social hour and dinner at the Hunt Memorial Building, 230 Scarborough Street, Hartford

5:30 SOCIAL HOUR

6:30 DINNER FOLLOWED BY A BUSINESS MEETING

SECTION ON OTOLARYNGOLOGY

3:30

Room 420

President: Howard W. Smith, *New Haven*

Secretary: Robert S. Rosnagle, *New Haven*

CRYOTHERAPY IN OTOLARYNGOLOGY

Cryotherapy for Nasal Hemorrhage

CHARLES D. BLUESTONE, *Pittsburgh, Pennsylvania*

Cryosurgery of the Tonsils

CHARLES L. HILL, *Providence, Rhode Island*

CONNECTICUT DISTRICT BRANCH—AMERICAN PSYCHIATRIC ASSOCIATION

3:30

Boston Buffalo Rooms

President: Lane Ameen, *New Haven*

Secretary: John H. Houck, *Hartford*

PSYCHIATRY FOR GENERAL PRACTITIONERS: THE CONNECTICUT PROGRAM

Panel: Austin McCawley, *Hartford*

Stephen Fleck, *New Haven*

John Donnelly, *Hartford*

Mr. Lee Isenberg, *Hartford*

SECTION ON RADIOLOGY

3:30

New York-Washington Rooms

President: Robert D. Russo, *Bridgeport*

Secretary: Orlando F. Gabriele, *New Haven*

CONSIDERATIONS IN THE MANAGEMENT OF LUNG CANCER

MORTON M. KLIGERMAN, *New Haven; Professor and Chairman, Department of Radiology, Yale University School of Medicine*

Thursday, April 28

CONNECTICUT SOCIETY OF AMERICAN BOARD SURGEONS

President: Malcolm M. Ellison, *New London*

Secretary: William A. Whalen, Jr., *Willimantic*

2:00-3:30 Terrace Room—Joint Meeting with Section on Orthopedics (See General Program—Thursday, 2:00 P.M.)

3:45 Bus trip to points of interest in Hartford

5:30 SOCIAL HOUR—Terrace Room

6:30 DINNER—Terrace Room

Guest Speaker: F. A. SIMEONE, *Cleveland, Ohio, Professor of Surgery, Western Reserve University School of Medicine, Director of Surgery, Cleveland Metropolitan General Hospital*

Title: RESEARCH AT THE BATTLEFRONT—WORLD WAR II AND THE KOREAN WAR

ASSOCIATION OF MEDICAL EXAMINERS FOR CONNECTICUT

President: Samuel B. Rentsch, *Derby*

Secretary: Francis P. A. Williams, *Monroe*

1:00 Rooms 436-440 Luncheon for Medical Examiners and Guests

3:30 BUSINESS MEETING

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SPECIAL NOTICE

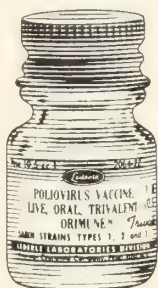
The combined medical and health council of the Connecticut Chapter of National Association of Social Workers, northern and southern sections, will be held on Wednesday, April 27, from 12:00 to 2:30 P.M. at the Shoreham Motor Hotel in Hartford. The topic to be discussed will be, "The Coming Role of the Social Workers as Liaison between Acute Hospitals and Extended Care Programs both Public and Private."



## TECHNICAL EXHIBITS

| <i>Space</i> | <i>Firm</i>                                             | <i>Location</i>      |
|--------------|---------------------------------------------------------|----------------------|
| 1            | G. D. Searle & Company                                  | Chicago, Ill.        |
| 2            | Mead Johnson Laboratories                               | Evansville, Ind.     |
| 3            | U.S. Vitamin & Pharmaceutical Corp.                     | New York, N.Y.       |
| 4            | Eli Lilly & Company                                     | Indianapolis, Ind.   |
| 5            | Arthur W. Eade Insurance Agency                         | Hamden, Conn.        |
| 6            | Surgeons' & Physicians' Supply Co.                      | Boston, Mass.        |
| 7            | Mayflower Securities                                    | New York, N.Y.       |
| 8            | Dome Chemicals, Inc.                                    | New York, N.Y.       |
| 9            | Encyclopedia Americana                                  | Needham, Mass.       |
| 10           | Ortho Pharmaceutical Corp.                              | Raritan, N.J.        |
| 11           | Organon, Inc.                                           | West Orange, N.J.    |
| 12-13        | Professional Equipment                                  | New Haven, Conn.     |
| 14           | Abbott Laboratories                                     | North Chicago, Ill.  |
| 15           | The Upjohn Company                                      | Kalamazoo, Mich.     |
| 16           | Sandoz Pharmaceuticals                                  | Hanover, N.J.        |
| 17           | Wallace Laboratories                                    | Cranbury, N.J.       |
| 18           | Mikel Electronics Co.                                   | Auburn, Mass.        |
| 19-22        | Connecticut Physicians' Art Association                 |                      |
| 23           | Merck Sharp & Dohme                                     | West Point, Pa.      |
| 24           | E. R. Squibb & Sons                                     | New York, N.Y.       |
| 25-26        | Connecticut Dairy and Food Council, Inc.                | Hartford, Conn.      |
| 27           | Brewer and Company, Inc.                                | Worcester, Mass.     |
| 28           | Connecticut Medical Political Action Committee (COMPAC) |                      |
| 29           | Encyclopaedia Britannica, Inc.                          | Chicago, Ill.        |
| 30           | Ciba Pharmaceutical Company                             | Summit, N.J.         |
| 31-34        | State Department of Health                              | Hartford, Conn.      |
| 35           | Flint Laboratories                                      | Morton Grove, Ill.   |
| 36           | Parke, Davis & Company                                  | Detroit, Mich.       |
| 37           | American Massage Equipment Company                      | Hackensack, N.J.     |
| 38           | Connecticut Heart Association                           | Hartford, Conn.      |
| 39           | Connecticut Committee on Medicine and Religion          |                      |
| 40           | Astra Pharmaceutical Products, Inc.                     | Worcester, Mass.     |
| 41           | 3M Business Products Sales, Inc.                        | West Hartford, Conn. |
| 42           | Brookes Research Associates                             | Hanover, N.J.        |
| 43           | The D. G. Stoughton Company                             | West Hartford, Conn. |
| 44           | Group Insurers, Inc.                                    | New Haven, Conn.     |
| 45           | The Emko Company                                        | St. Louis, Mo.       |
| 46           | Equity Investment Corporation                           | New Haven, Conn.     |
| 47           | Lessere-Wertheim, Inc.                                  | Hartford, Conn.      |
| 48           | The Stuart Company                                      | Pasadena, Calif.     |
| 49           | Syntex Laboratories, Inc.                               | Palo Alto, Calif.    |

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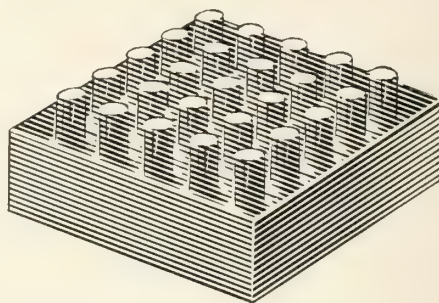
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In infants vaccination should not be commenced before the sixth week of life. Do not give to patients with viral disease, or if there is persistent diarrhea or vomiting. ORIMUNE and live virus measles vaccine should be given separately.

Dosage—initial immunization: two doses each given orally at least 8 weeks apart. (Give a third dose to infants at 10-12 months). Booster immunization: one dose, given orally. See package literature for full directions.



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Side effects are possible but rare: vesiculation, ulceration or necrosis at test site. Contraindications, none; but use with caution in active tuberculosis. Available in boxes of 5 (new individually-capped unit); cartons of 25.

\*Rosenthal, S. R., Nikurs, L., Yordy, E., and Williams, W.: Scientific Exhibit Presented at the Annual Meeting of the National Tuberculosis Association, Chicago, Illinois, May 30-June 2, 1965.

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# THE PRESIDENT'S PAGE

## AMERICAN MEDICAL ASSOCIATION DUES INCREASE

**A**T the Clinical Convention of the American Medical Association held in December 1965 in Philadelphia, the House of Delegates approved a recommendation of the Board of Trustees to increase the membership dues from forty-five to seventy dollars. This approval was made subject to final action by the House at the Annual American Medical Association Convention in June 1966.

The Board of Trustees' recommendation for the dues increase was based on the same problems that confront every practicing physician and every firm that is engaged in business in this country today, namely, a continual rising spiral of costs which in recent years has cut in half the purchasing power of the dollar. In the vital area of communication alone an increased cost of 181 percent has occurred in the past five years. American Medical Association real estate taxes have been increased almost 200 per cent since 1959. Salaries and employee benefits have risen 25 percent as in all industry, and the society must compete with business for competent people to carry on its affairs. With the advent of Medicare, Social Security taxes will rise from \$160,000 in 1960 to \$276,000 in 1966.

The American Medical Association organization has been growing in recent years to keep abreast of all the problems confronting medicine and to bring the ever expanding wealth of medical knowledge to its members and the public. It cannot continue this needed development on yesterday's income. Somewhat less than 28 per cent of AMA income will be derived from dues in 1966 if the dues remain at \$45. Over sixty per cent of income comes from other sources such as subscriptions, exhibit spaces at meetings, advertising and investments.

Expenses would be much higher if it were not for the free time given by the hundreds of physicians who serve on the Councils, commissions, committees and allied groups, that with the staff carry on the tremendous tasks that the AMA handles every year. With the advent of government financing in the field of medicine, the Society's tasks will be more arduous than ever, but they must be done. The necessary dues increase at this time for all of us will help our national organization carry out the many responsible tasks we ourselves, the government and the people assign to the American Medical Association.

JAMES R. CULLEN, M.D.

# MAJOR MEDICAL EXPENSE PLAN



## A NEW SPECIAL ENROLLMENT PERIOD ALLOWS YOU TO APPLY FOR AN IMPROVED CONTRACT

Reimbursements up to \$10,000.00. Deductible of \$500.00, \$750.00, or \$1,000.00. Protection after retirement, coverage for widows and children in the event of prior demise of member. All dependent children can be covered regardless of age. This same broad coverage is also available for the first time to your employees and their families.

## ACCIDENT AND HEALTH PLAN

In addition to the above, members up to age 40 may now purchase their Accident and Health protection at a 25% reduction in cost.

Through its continued official sponsorship of our Group Plans, The Connecticut State Medical Society has once again made it possible to offer broadened coverage under these two time-tested policies to members of the Society. If you are not now enrolled, do not turn your back on old friends who have served Connecticut physicians for over a quarter of a century. If a sufficient number of new applications are submitted for the Major Medical Expense Plan, all policies will be issued regardless of past medical history. For full information write or phone.

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# The All Wire Technique In Wound Closure

Marvin S. Arons, M.D., D.M.D.

## Introduction

■ It has been pointed out that the method of using the stitch in skin closure is of much greater importance than the suture material. The general principles of plastic surgery as applied to wound closure include: careful hemostasis, removal of devitalized tissue and foreign bodies, obliteration of dead space, prevention of hematoma, right angle incisions, following the lines of tension for incisions, relaxation of the skin edges, coaptation of skin edges without tension, early and progressive removal of sutures with subsequent skin edge support, and gentle and meticulous surgery with the use of fine non-irritating suture materials.

Through the centuries, four major methods for the approximation of wounds have been employed. These are: (1) bandaging, (2) strips of adhesive materials, (3) clips, hooks and needles, and (4) the needle with suture. The last has survived as the dominating procedure of choice with most surgeons in all specialties. The introduction of a variety of suture materials and improvements in preparation have not produced a suture that meets all the ideal standards and requirements. Nor is this presentation designed to evaluate the efficacy of one suture as opposed to another or to discuss the problem of the healing of skin wounds. For information in this area, the reader is referred elsewhere in the literature. Rather, one method that has been found useful in closing accidental or elective wounds and which attempts to meet the criteria for the plastic surgical closure of all wounds is being presented.<sup>1</sup>

## Procedure

Diagrammatically in Figure I, the all wire closure of an elliptical shaped wound is illustrated. The edges of the defect have been undermined and hemostasis secured with No 40. stainless steel wire ties. These ties are best secured using a straight mosquito hemostat. On a curved cutting needle, No. 36 stainless steel wire stent sutures are passed as seen in (1). It is imperative that these sutures be passed through the deepest part of the defect since in this way they help obliterate dead space in the final closure. The ends of these stent wires are then secured with hemostats to prevent loose ends from interfering with the remaining part of the closure. The next step as seen in (2) is the suture of the wound with a continuous No. 36 subcuticular pull-out wire. In using a subcuticular pull-out

wire, it is necessary to pull on each end of the wire after each passage through the tissue in order to prevent kinking which would later interfere with its removal. All the wires are now in place as seen in (3). Depending upon the area, No. 4-O, No. 5-O, or No. 6-O black silk is then used to close the skin edges which should be well aligned and together even before these final sutures are placed. These silk sutures are used only to coapt the edges of the wound to get an even more precise wound closure and should not be placed under tension. In this regard, the first knot is always the most important when square knots are utilized. Either Furacin, Xeroform, or glycerine impregnated fine mesh gauze is placed next to the wound. Any such material which is hygroscopic and water soluble helps prevent crusting in the wound which also promotes faster healing and less scarring. Finally, as seen in (5), several gauze sponges are trimmed, rolled, and placed against the wound. The stent wires are then securely tied over them and the subcuticular wire also is loosely tied over. In addition to obliterating dead space, the stent wires reduce tension on the wound edges and also secure a firm pressure dressing in place. Often, no further dressing is required especially in the area of the face. Post-operatively,

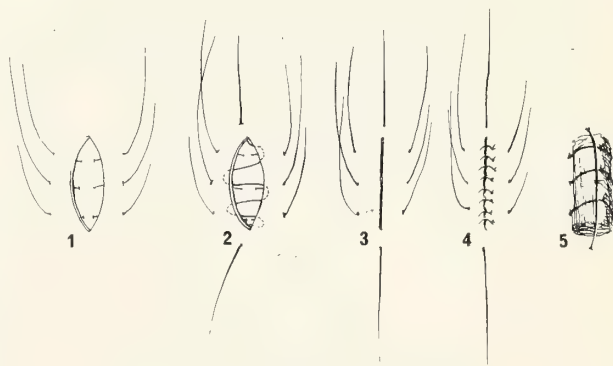


FIGURE I

Diagrammatic representation of all wire closure of an elliptical wound of the skin.

DR. MARVIN S. ARONS, associate surgeon, Yale-New Haven Medical Center, New Haven, Conn.; junior assistant attending surgeon, St. Raphael's Hospital, New Haven, Conn.; attending plastic surgeon, Veterans Administration Hospital, West Haven, Conn.

the stent dressing and the stent wires are removed on the third post-operative day. At this time, progressive removal of the black silk sutures has begun. One-third of these sutures are removed on the third post-operative day, another third on the fourth post-operative day, and all remaining silk skin sutures are removed on the fifth post-operative day. The ends of the subcuticular pull-out wire are curled on the end of a straight hemostat so as to prevent loose ends. Now the main mechanical support of the wound resides in the subcuticular pull-out suture which may remain in for a variable period of time depending upon the location of the wound and whether or not subcutaneous buried wire sutures were utilized. As an example, if the wound were over the anterior tibial area, No. 36

or No. 38 interrupted buried wire subcutaneous sutures would have been tied in place prior to the insertion of the pull-out wire. The removal of the pull-out wire would be approximately on the fourteenth post-operative day. If this were a small lesion or wound of the face, the subcuticular wire probably would be removed on/or about the ninth post-operative day.

### Conclusion

An all wire technique for closure of accidental and elective surface wounds of the body has been presented.

### Reference

1. Blocker, T. G., Jr. and Lewis, S. R.: Personal Communication.

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## NARCOTICS — TREATMENT AND THE LAW

HALL OF THE HOUSE OF REPRESENTATIVES

State Capitol Building, Hartford

APRIL 21, 1966

AFTERNOON SESSION — 2:30-5:00 P.M.

EVENING SESSION — 7:45-10:00 P.M.

CO-MODERATORS: STATE SENATOR FREDERICK POPE, JR., *Fairfield*

STATE SENATOR GLORIA SCHAEFFER, *Woodbridge*

### SPEAKERS:

DR. DAVID MEYERSON, Professor, Harvard Medical School, Director, Massachusetts Narcotics Treatment Service, Cambridge Massachusetts  
SHERMAN PATRICK, Director, HAR-You Youth Program, New York City  
SAMUEL LEVINE, District Supervisor, Federal Bureau of Narcotics, Philadelphia, Pennsylvania

### SPEAKERS:

DR. JOHN DONNELLY, Psychiatrist-in-Chief, Institute of Living, Hartford  
HENRY DISUVERO, Staff Counsel, New York Civil Liberties Union, New York City  
HAROLD L. PATTON, Connecticut Consultant, National Council on Crime and Delinquency Monroe, New York

PANEL DISCUSSION—9:00-10:00 P.M.

### Co-Sponsors:

ALCOHOLISM DIVISION, DEPARTMENT OF MENTAL HEALTH; CONNECTICUT ASSOCIATION FOR MENTAL HEALTH; THE CONNECTICUT CIVIL LIBERTIES UNION; CONNECTICUT COUNCIL OF CHURCHES; CONNECTICUT JEWISH COMMUNITY RELATIONS COUNCIL; CONNECTICUT STATE MEDICAL SOCIETY; HARTFORD CATHOLIC INTERRACIAL COUNCIL; HARTFORD COUNTY MEDICAL ASSOCIATION; NATIONAL ASSOCIATION OF SOCIAL WORKERS, NORTHERN CONNECTICUT CHAPTER; AND UNITARIAN UNIVERSALIST ASSOCIATION, CONNECTICUT VALLEY DISTRICT.

### THE GENERAL PUBLIC IS INVITED

Admission is Free — Approved by the American Academy of General Practice for five hours of Category 2, Post Graduate Educational Credit.



# Meigs' Syndrome – An Incomplete Form With Severe Hydrothorax

Terence F. McNulty, M.D. and John A. Muccino, M.D.

■ The first mention of an association of an ovarian tumor with hydrothorax was made by Spiegelberg in 1866, followed by Gaillard Thomas in 1877. However, Cullingworth in 1879 was the first to report a case of ovarian fibromata with ascites and pleural effusion. In 1829, Lawson Tait emphasized that the Association of hydrothorax, ascites, and abdominal tumor did not always signify malignancy as was formerly upheld.

In the United States in 1937 seven cases were reported by Meigs and Cass, and in the same year Rhoads and Terrell designated the syndrome after Meigs. The first mention of the syndrome in the American literature was by Spencer Wells in 1882; but it was not until after the publication of Meigs' and Cass' collected cases that the syndromes became universally recognized.

Since the original communications in the British journals by Cullingworth and Lawson Tait, cases have been reported by Borg (1941), Gild (1943), Clay, Johnston and Samson (1944), Gardiner and Lloyd-Hart (1944), Lawlor (1944), Erez (1945), Marshall (1949), Lawson (1950), Conway-Hughes (1951), and Blair in 1961. Although Meigs has made the major contribution to the collection and research of this syndrome, he reported in 1954 that the more correct name should be the "Demons'-Meigs' syndrome," since Demonds reported cases in 1887, 1902 and 1903. In 1954, Meigs presented a collection of 84 such cases. Meigs' observations and reports have aroused interest in this syndrome everywhere.

In Meigs' original description of the syndrome the following conditions were necessary for the use of the term "Meigs' syndrome": (1) Presence of an ovarian fibroma, (2) hydrothorax, (3) ascites, and (4) cure after extirpation of the ovarian tumor. He originally limited the term to ovarian fibromas. However, reports on benign ovarian tumors of different pathogenesis associated with ascites and hydrothorax that were cured after surgical extirpation of the tumor have extended the use of the term "Meigs' syndrome." In the world literature, the syndrome has been described in a uterine myoma, a papillary cystadenoma of the ovary, a blastoma, a granulosa-theca cell tumor and a Bren-

ner tumor. Meigs' cases included theca cell, granulosa cell and Brenner tumors, benign ovarian tumors including cysts, uterine myomas, a tubal papilloma, and two cases of struma ovarii. Occasionally the syndrome has been observed in malignant, solid, non-metastasizing genital tumors. Meigs has definitely excluded dermoid cysts and teratomas from the syndrome. In 1961 Blair reported a case of Meigs' syndrome which had added features of interest. In addition to an ovarian fibroma, there was a Brenner tumor of the opposite ovary, a small carcinoma in a fallopian tube, together with multiple uterine fibromyomata and cystic glandular hyperplasia of the endometrium.

Meigs' syndrome is relatively uncommon and mimics the terminal phase of a metastasizing malignant tumor, far advanced cirrhosis or cardiac failure but is curable by surgical treatment. The syndrome is actually a triad of ovarian fibroma, ascites and pleural effusion. Every woman with ascites and hydrothorax should be very carefully examined for the possible presence of ovarian tumor. If one is found, laparotomy should be performed. The decision to perform this operation may require firm resolution on the part of the gynecologist, as he may find his opinion opposed by the internist or general surgeon. Very often a patient with Meigs' syndrome will, because of her hydrothorax, present herself to the internist, and even the textbooks of medicine have not included this syndrome among the causes of hydrothorax.

It has been found that malignant ovarian tumors are also capable of producing the syndrome. In 1952 several writers collected 17 cases from the literature in which malignancy of the ovary was associated with Meigs' syndrome.

Meigs divided the conditions in which removal of the tumor causes disappearance of the collections of fluid in the abdomen and thorax into four categories: (1) *true* Meigs' syndrome, (2) ovarian benign cysts such as liomyoma, teratoma (3) ma-

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DR. TERENCE F. McNULTY, associate obstetrician and gynecologist, St. Francis Hospital, Hartford, Conn.

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FIGURE I  
Chest roentgenogram before surgery.

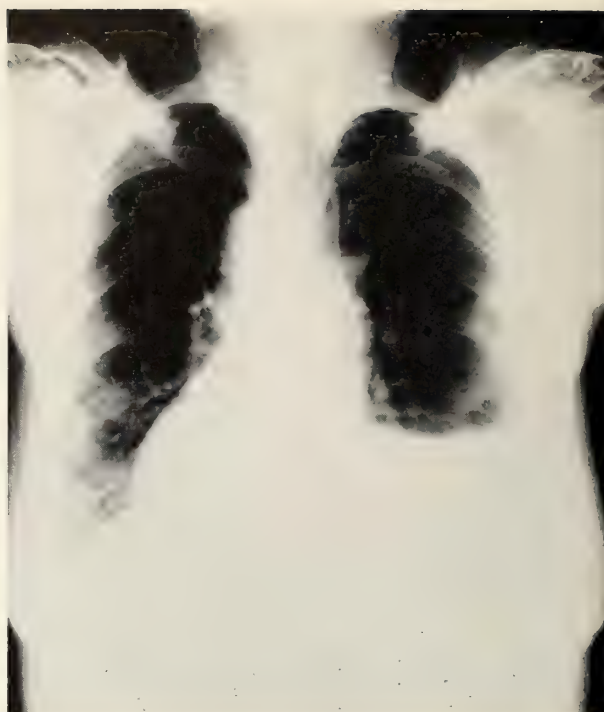


FIGURE II  
Chest roentgenogram before discharge from hospital.

lignant ovarian processes, (4) cystic, traumatic, and carcinomatous changes of the pancreas.

The "true" Meigs' syndrome is associated with the following: (1) ovarian fibroma or fibroma-like tumor, (2) ascites, (3) hydrothorax, (4) the latter disappear with the removal of the ovarian tumor.

The viewpoint that Meigs' syndrome is an association of ovarian tumor with ascites and hydrothorax which can be cured by ovariectomy is shared by the present authors. Possibly, also to be included are the rare cases of myoma of the uterus or benign pelvic tumor in which this symptom complex occurs. However, they do not agree with those who consider Meigs' syndrome as any polyserositis which can be cured by removal of either a benign or a malignant ovarian tumor. The present authors consider the benignity of the process one of the chief criteria. Therefore, histologic examination of the tumor is important.

There have been cases in which the malignancy of the process was undoubted. Such was the case in which, in addition to a Krukenberg tumor with ascites and hydrothorax, the first symptom—i.e., the one which led the patient to the physician—was hematemesis (stomach metastasis); and the palliative operation, namely oophorectomy, resulted in the disappearance of the increased body fluid. This condition has been called "Pseudosyndrome of Meigs." The treatment in both conditions is the same, namely prompt laparotomy and ovariectomy. The problem of differentiating a true Meigs' syn-

drome from a Pseudo-Meigs' syndrome remains the work of the histologist.

Leger and Roy (1949) and later Blair (1961) employed the term "incomplete form of Meigs' syndrome," in describing cases with hydrothorax without obvious ascites. Such is the case reported by the present authors here:

#### Case Report

The patient is a 67-year-old, multiparous white, married female, eight years postmenopausal, admitted to Saint Francis Hospital as an emergency on June 16, 1965 with a history of severe cough, with bouts of breathlessness, and pain in the right chest of six week's duration. Past history revealed treatment for "hypertension and heart failure," in February, 1956, and vaginal hysterectomy for "Prolapse" in 1957.

On admission, the patient appeared well-nourished and well-developed, but pale and dyspneic. The blood pressure was 160/90; the temperature was 99°F. There were no pulsating neck vessels. The right side of the chest lagged on inspiration and expiration and was dull to percussion from the level of the seventh thoracic vertebra to the inferior thoracic margin. Breath sounds were absent from this area. The heart was not enlarged and no murmurs were heard. The abdomen was tense, but no fluid wave was elicited. Dullness was noted in the right lower quadrant. A firm, fixed, non-tender mass was palpable in the right lower quadrant from the symphysis pubis to the right iliac crest. Pelvic examination revealed a normal vagina and no cervix. A firm, slightly irregular, slightly moveable, non-tender mass was palpated in the right adnexal region and filled the cul-de-sac. Complete blood count and urinalysis were within normal limits. Blood sedimentation rate was 43 mm/1 hr.





FIGURE III  
Whole specimen.

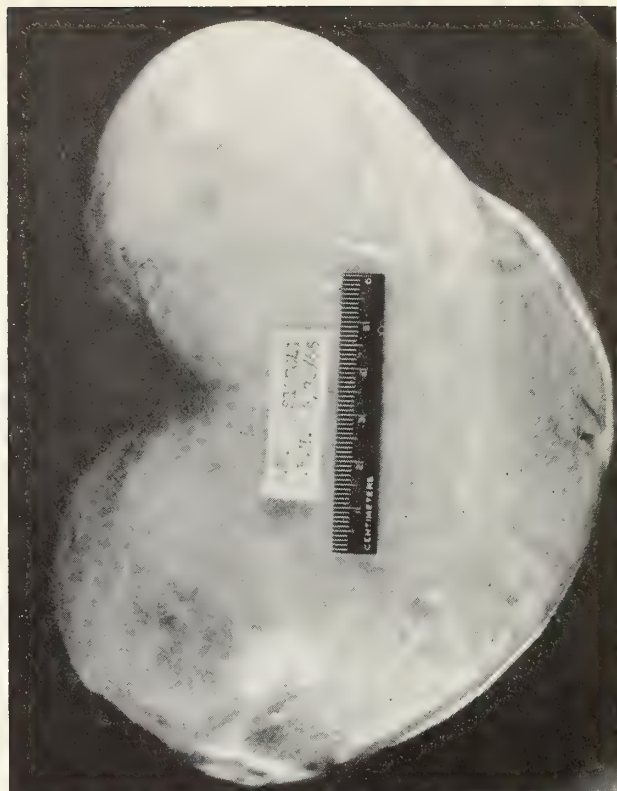


FIGURE IV  
Cross-section of specimen.

A massive right-sided pleural effusion was diagnosed on clinical examination and confirmed by radiography. The patient had repeated chest aspirations, a straw-colored lymphocytic fluid being withdrawn, which relieved her dyspnea. Pathologic examination of the chest aspirate revealed no malignant cells, and smears were negative for tubercle bacilli. Cultures revealed no growth. A total of eight liters of fluid was aspirated from the right chest. The patient improved subjectively and was ready for laparotomy, which was performed on the fourteenth hospital day. No fluid was present in the peritoneal cavity. A large, solid, horse-shoe shaped mass was arising from the right ovary, grayish-white in appearance, encapsulated and measuring 20 cm. in its greatest dimension. The right tube and the left tube and ovary were normal. The remainder of the abdomen, on exploration, was normal. No uterus was present; and the cuff was well-healed. A right oophorectomy was performed. The pathological diagnosis was fibroma of the right ovary. The patient's post-operative course was uncomplicated. Clinically, and radiographically, the right lung cleared, and the patient was discharged from the hospital on the ninth post-operative day. Figures show chest X-rays before and after surgery, and photographs of the specimen are included.

### Discussion

The case presented represents a case of an "incomplete form of Meigs' syndrome" with ovarian fibroma, massive hydrothorax but no ascites.

The true syndrome's symptom complex of ovarian fibroma, hydrothorax and ascites occurs chiefly in women in the menopause, but has been observed in patients between the ages of 9 and 88 years. No connection to number of pregnancies or birth has been found. The early symptoms are dyspnea, loss of weight, a feeling of weakness, inappetence, enlargement of the abdomen, and, finally, cough. The patients may erroneously be treated for cachexia due to malignancy or for heart or lung disease.

The size of the ovarian tumor may vary from that of a hen's egg to that of a child's head. There is no relationship between the size of the tumor and the degree of the fluid collections. The ascites may vary in amount between 100 cc. and 1,000 cc. The hydrothorax may be considerable. It may be unilateral or bilateral. Fluid which is removed is very rapidly replaced. The removed fluid is clear, its protein content is low; usually it is a transudate with a specific gravity of less than 1.015. The aspirate contains little sediment which consists of lymphocytes, monocytes, or endothelial cells. When one obtains a bloody aspirate, this does not rule out Meigs' syndrome. It may be due to necrosis or torsion of the tumor and its presence does not remove the necessity for laparotomy.

The tumor is directly or indirectly the cause of the ascites and the hydrothorax. Regardless of whether the fluid reaches the pleural cavity by way of the lymphatics or whether there is a direct communication between the abdominal cavity and the thorax, it is not clear why a very slight ascites may be associated with a large hydrothorax. It is also not known why the hydrothorax affects only the right or the left side of the chest. Several authors are of the opinion that the development of ascites and hydrothorax in association with Meigs' syndrome is due to the simultaneous action of several factors. In addition to the mechanical effect, there is the possibility of relative or absolute metabolic disturbance (catabolism) which may cause increase of the hydropic (steroid) substance secreted by the tumor and possible changes in the reactions of the serosa. Certain conditions (such as developmental variations of the lymphatic system, or communication between the two body cavities) may also determine whether there is hydrothorax in addition to ascites and on which side it will be localized.

Of interest is the notation that roentgen irradiation of the tumor will cause disappearance of the ascites and hydrothorax. The mechanism of action of roentgen ray therapy, aside from its shrinking affect on the tumor, is possibly the blocking of the discharge from the tumor, of edema-rendering substances of the tumor cells. The treatment also possibly stimulates absorption. However, irradiation therapy, in spite of the good results, cannot replace laparotomy in the treatment of Meigs' syndrome. It should replace surgery only in cases where there is an absolute contraindication to operation, where it is impossible to operate, or where the patient refuses an operation. In such cases, the irradiation therapy can prevent recurrence of ascites and hydrothorax, and time is gained so that laparotomy may be done later under more favorable conditions.

## Summary

1. A brief account of the history and features of Meigs' syndrome is given.

2. A case of "incomplete form of Meigs' syndrome" is reported.

3. The signs, symptoms, and pathophysiology is briefly reviewed.

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The truly scientific spirit should make us modest and kindly. We really know very little and we are all fallible when facing the immense difficulties presented by investigation of natural phenomena.

—Claude Bernard, M.D., *An Introduction To The Study Of Experimental Medicine*.



# Alaryngeal Voice Production

Jay W. Lerman, Ph.D.

■ "The complete loss of voice in laryngectomy . . . is a basic threat to the integrity of the person. It will provoke unendurable and thoughtless penalties and deprivations."<sup>1</sup>

In today's communication-conscious world the ability to verbalize one's thoughts is a necessity. Following removal of the larynx, an individual is subjected to a severe emotional shock with the realization of his inability to talk as he has in the past. Feelings of depression and helplessness which frequently arise during the period of convalescence may be further reinforced by exaggerated or oversollicitous reactions on the part of the patient's family.

Invaluable aid can be given in the rehabilitation of these patients and the counseling of the families. If at all possible, the surgeon and the speech pathologist should prepare the patient and family for the after-effects of the surgical procedure. This will not necessarily eliminate, but may help reduce the severity of the shock following surgery. Of further importance and reassurance would be the knowledge that while the normal avenue of communication will no longer be open to the patient, there are substitutes which will allow him to communicate—and communicate verbally.

Essentially two methods are available: the development of alaryngeal speech and/or the use of an artificial larynx. While the development of alaryngeal speech, particularly esophageal speech, is preferred, the use of an artificial larynx need not and should not be eliminated. Such an instrument may be used as a temporary measure to provide communication immediately after surgery and for later use as a supplementary tool.

There are two types of artificial larynx: the pneumatic type (pulmonary air from the stoma), and the electric larynx (operated by battery). Of the pneumatic or mechanical type the most common has been the metal reed or "reed" type larynx. Essentially this is a tube, one end of which is fitted over the tracheal opening and one end placed in the mouth. The air stream, coming from the neck opening, is passed through the tube, setting into vibration a reed contained in the tube. These vibrations are conveyed into the oral cavity where articulation of the sound occurs.

The electrolarynx is a vibrating mechanism electrically driven with current supplied by batteries. In most cases the vibrating mechanism con-

sists of a diaphragm encased in a tube. The diaphragm is placed against the throat. When the current is turned on, it vibrates the diaphragm and produces a buzzing sound. This buzzing noise acts in a fashion similar to vibrating vocal folds. In a sense, the buzzing sound passes into the oral cavity where it is then articulated into sounds and words.

Both of these systems, mechanical and electric larynx, have a number of disadvantages: the instrument must be carried and available at all times; it is rather conspicuous and constantly reminds the individual of his disability; the instrument is subject to breakdowns and in such case requires immediate care, leaving the individual without speech; the voice quality is generally metallic with little pitch variation, making for a monotonous quality. There have been some references, too, to differences in intelligibility between esophageal speech and speech using an artificial larynx, but further definitive research is needed.

There is, however, one significant advantage to such an instrument: it can take only a few hours to learn to use, thereby giving the laryngectomized individual almost immediate communication. In addition, there are other conditions which may indicate the use of the artificial larynx over the usually preferable esophageal speech: in an elderly patient it may be more expedient, in consideration of his anticipated longevity of life; and where there are some physical impediments such as excessive scarring, inert status (paralysis), flaccidity (no tone or quality to movement), paucity of tissue (particularly of the cricopharyngeus muscle), and massive extirpative operation, the use of esophageal speech would be precluded.

Where alaryngeal voice can be developed, three types of classes are possible: pharyngeal, buccal, and esophageal.

In pharyngeal speech, the air is trapped in the hypopharynx. The tongue may be positioned against the pharynx, with the point of vibration being at the (a) pharynx, (b) palate, or (c) pillars of Fauces. In utilizing this type of alaryngeal voice

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there is generally poor control of the articulatory mechanism, particularly the tongue. This leads to poor articulation and poorer intelligibility of conversation speech.

A second class of alaryngeal speech has been called buccal speech. The voice is produced in the foremost part of the oral cavity, utilizing air from an air reservoir between the maxillar surface and the cheek. It is produced by buccolingual compression of this air. There have been differences of opinion with regard to the description of this type of speech. At times it is a whispering type of speech which may be spontaneously developed, hence referred to as a "buccal whisper"; on other instances it takes on a distinctive quality which has merited its description as "Donald Duck" speech. In both types, however, the speech is generally not loud enough and has poor intelligibility.

The most commonly used and most preferred type of alaryngeal voice is the esophageal voice. In this type of pseudovoice the air supply is trapped in the esophagus usually at the level of the fourth to sixth cervicle. The cricopharyngeal muscle then becomes the new voice muscle. However, the cricopharyngus is not the only structure involved in vibration during esophageal speech. Other organs concerned with the vibration of the pseudoglottis are superior esophageal constrictor and the pharyngo-esophageal segment. The most efficient esophageal voice is that in which the air supply is available from the esophageal area rather than the air supply from the stomach.

Esophageal speech has certain advantages over an artificial larynx: it has greater pitch variability; it is not as conspicuous and does not call as much attention to itself; it is good psychologically, in that it is more natural and may allow the patient to feel that he can compete as a "normal" person; and, there are no mechanical breakdowns.

Its disadvantages are that it is not too powerful in volume; it cannot be learned by all; it is sometimes difficult to learn; and, until it is learned, it delays the person's communicative ability and therefore may cause frustration or even defeat its own purpose.

In teaching esophageal speech, the attitude of the patient is very important, and not infrequently a problem. "The psychological effect of enforced silence during a protracted learning period for esophageal speech is the building of resentments and frustrations that tend to make the patient uncooperative."<sup>2</sup> As previously stated, a negative attitude on the part of the patient may be minimized by pre-operative preparation by the surgeon and the speech pathologist, along with continued counseling of the patient and his family.

The initial step in developing esophageal speech is the intake of air. There are basically three methods of trapping air: (1) inhalation, (2) injection, (3) swallowing. Any of these methods is satisfactory, provided the air is not completely "swallowed" and stored in the stomach. Once the air has been taken in, the next step is the expulsion of the air.

The terms "belch" and "burp" have often been used in referring to and describing esophageal speech. While many people, both the laryngectomized individuals and speech pathologists, have reacted negatively to such terminology, the use of these terms can prove invaluable as a therapeutic tool. The universal familiarity with burping or belching makes it a quick, unambiguous, vivid reference for the patient, and in the primary stages of therapy can be an excellent starting point. Although the approach is a very simple one, it can be met with early success and give reassurance, confidence and optimism. For the individual who has belched naturally since his operation, the prognosis for eventual speech would probably be very good. With others for whom the production of a "belch" will be difficult to obtain, the speech pathologist will have to resort to other therapeutic techniques. However, once the "belch" can be produced voluntarily on command, it should then be referred to as the esophageal sound or esophageal speech.

When the sound can be produced at will, the next step is to attempt production of vowel sounds. Following a period of practice and success on the vowels, they may be combined with voiceless consonants, which do not require esophageal sound but rather the air already in the oral cavity (particularly the p,t,k, and s) to form short words and syllables. From words the individual will go to short phrases, sentences, and conversation.

It must be noted that esophageal speech is not an easy process to learn. The simplicity with which it is explained here is not indicative of the difficulties which can be encountered in the therapeutic process. Progress in many instances can be slow and ungratifying. However, it *has* been learned and mastered by many, and when it is, it is an achievement of the closest approximation of normal verbal communication, a socially satisfying accomplishment, and a personally gratifying one.

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# Shoulder Pain As A Presenting Complaint In Upper Lobe Bronchogenic Carcinoma: Report Of 21 Cases

Richard M. Engelman, M.D.

## Introduction

■ Among the many hundreds of patients admitted to hospitals annually with complaints referable to bronchogenic carcinoma, a small but important fraction begin their course with shoulder pain, and sometimes insufficient attention, on the part of the patient or physician, is paid to this symptom as a manifestation of disease in the lung. Delay may arise in diagnosis and treatment, and inevitably certain patients are submitted to prolonged local treatment with physiotherapeutic measures or intraarticular injections with a mistaken diagnosis, for example, of subdeltoid bursitis or peripheral neuritis.

An illustrative case was a patient treated for a year and a half with analgesics under the mistaken diagnosis of "osteoarthritis."

## Case History No. 1

O. M., a 74 year old white male, had right shoulder pain for approximately eighteen months with numbness, weakness and muscle wasting in his right hand for the last two months. He subsequently developed generalized weakness, confusion and disorientation. Right-sided Horner's syndrome was noted on physical examination.

Admission chest x-ray revealed an infiltrate in the apical region of the right upper lobe with destruction of the lower cervical and upper thoracic vertebrae and involvement of the first three ribs on the right side (Figure I). The patient succumbed unexpectedly before any specific therapy could be instituted. No postmortem examination was performed.

Patients with lung tumors situated in the apex of the lung have long been known to have associated shoulder pain, as the previous case illustrates.<sup>1</sup> However, occasionally a centrally located tumor\* in either of the upper lobes may present with shoulder pain.

## Case History No. 2

S.A., a 75 year old Negro male, had a three month history of pain beginning in the left shoulder and radiating down the left arm. He had also noted right chest pain, a productive cough, anorexia and weight loss. No Horner's syndrome was present, but the patient did have a palpable right axillary lymph node, cyanotic nail beds and crackling basilar rales bilaterally.

\* Definition of a central tumor—One which is located at the main stem, lobar or segmental bronchial level.

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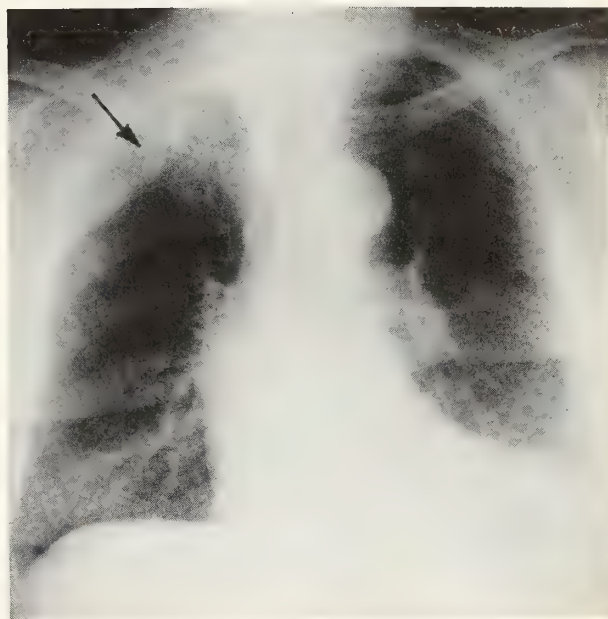


FIGURE I

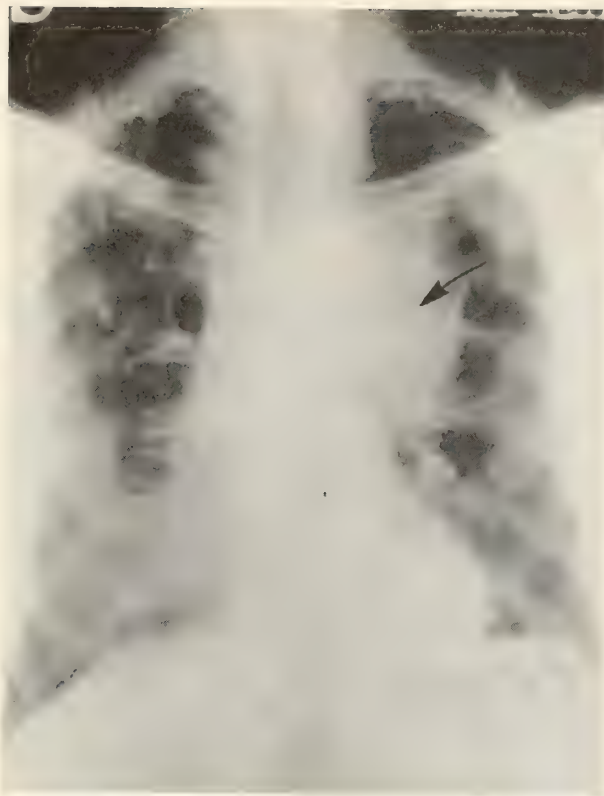
P.A. chest film reveals a right apical lesion. There is destruction of the first two ribs on the right with fracture of the third.

Chest x-ray revealed a left hilar density with atelectasis of the left upper lobe, multiple nodules in the right lung and partial destruction of the fifth rib bilaterally (Figures II and III). An axillary lymph node biopsy revealed undifferentiated carcinoma; chemotherapy with nitrogen mustard was begun. The patient, however, continued on a downhill course and developed a pathologic fracture of his left femur. He subsequently aspirated during a feeding and died shortly thereafter.

Postmortem examination revealed tumor in the superior division bronchus of the left upper lobe with distal atelectasis and abscess formation. The growth involved the pleura, invaded the mediastinum and had insinuated itself around the aortic arch. The histologic diagnosis was epidermoid carcinoma. Metastatic sites included the ribs, right lung, liver, right adrenal, kidneys, pituitary and thyroid.

The present investigation sought to analyze a consecutive series of one hundred and fifty upper lobe bronchogenic carcinomas in order to determine the incidence of shoulder and arm pain as a

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FIGURES II AND III  
P.A. and lateral chest films show a left upper lobe parahilar density.

presenting complaint (i.e., a major symptom when first seen for diagnostic study in this hospital) and to evaluate the therapy employed and results. The case histories were taken from all services of the Grace-New Haven Community Hospital during the period 1960-64.

The total number of patients in this series who presented with a complaint of shoulder, scapular or arm pain was twenty-one, or 14 per cent of the one hundred and fifty cases. Additional presenting symptoms included, in descending order of frequency, cough, chest pain, neck pain, dyspnea, weakness, weight loss, anorexia, wheezing, swollen facies, numbness or tingling in the fingers, muscular weakness in the arm, hemoptysis, hoarseness and fever.

There were seventeen males who ranged in age from 35 to 79 years and four females who ranged from 49 to 67 years. The average length of time which elapsed between the onset of the initial

symptom and the diagnosis was 5.2 months. The average period between the diagnosis and death was 5.7 months (Table I). One female patient is presently living.

Haas, et al<sup>2</sup> in their series of eighteen apical lung tumors found an average of 10.1 months between the appearance of the initial complaint, which was most frequently shoulder pain, and the diagnosis. In McNeill's<sup>3</sup> review of 700 cases of bronchogenic carcinoma, the mean duration between initial symptom and diagnosis was 8.4 months. In the latter, which was a general review of lung cancer, he found shoulder pain to be the earliest symptom in 3 per cent of cases.

### Diagnosis

The various tests generally employed in the diagnosis of suspected bronchogenic carcinoma include radiography, sputum cytology, bronchoscopy and scalene lymph node biopsy (Tables II and III). A study of these twenty-one cases reveals that four had tumors centrally located in the upper lobe, an incidence of 19 per cent. In the remaining seventeen cases, the tumor was present in the periphery of the upper lobe. The right side predominated in a ratio of 3.2 to 1. In the cases where the tumor could be segmentally localized, the apical segment significantly outnumbered the other segments. It was radiologically apparent that thirteen of the

TABLE I  
DURATION OF SYMPTOMS

|                                                           | RANGE IN MONTHS | AVERAGE |
|-----------------------------------------------------------|-----------------|---------|
| From first symptom to first diagnosis in twenty-one cases | 1 to 24         | 5.2     |
| From first diagnosis to death in twenty cases             | 0.5 to 35       | 5.7     |



TABLE II  
X-RAY LOCALIZATION OF TUMOR

| PERIPHERAL LOCATION |                            | NUMBER OF CASES |
|---------------------|----------------------------|-----------------|
| By Lobe:            | Right upper lobe           | 13              |
|                     | Left upper lobe            | 4               |
| By Segment:         | Apical or apical-posterior | 10              |
|                     | Anterior                   | 3               |
| CENTRAL LOCATION    |                            |                 |
| By Lobe:            | Right upper lobe           | 3               |
|                     | Left upper lobe            | 1               |

cases (62 per cent) probably had hilar or mediastinal lymph node metastases.

A positive tissue diagnosis was made in nineteen of the twenty-one cases (Table IV). The most common types of carcinoma noted were undifferentiated and epidermoid carcinoma with seven instances of each.

Several of the published reports relating shoulder pain and bronchogenic carcinoma describe the cell type of carcinoma present.<sup>4-10</sup> These cases, of which there are thirty-nine, indicate a slight preponderance of squamous cell carcinoma (nineteen cases of squamous cell carcinoma, fifteen cases of adenocarcinoma and five of undifferentiated carcinoma).

### Treatment

The various modalities of treatment used in these twenty-one cases are noted in Table V. In seventeen of the twenty-one (81 per cent), the tumor was surgically unresectable when the patients were first hospitalized. Most of these cases were treated with radical irradiation therapy or palliative techniques. The remainder received no specific therapy.

Four cases were treated surgically. Two of these, a lobectomy (M.G.) and a pneumonectomy (W.Y.), died in the immediate post-operative period, the former with multiple small pulmonary emboli and the latter with right-sided heart failure. The remaining two cases survived from 8 to 11 months with considerable symptomatic relief.

The patients who received only palliative treatment may be divided into three groups, depending upon subjective response: those who were significantly improved (one case), those whose symptoms were slightly relieved (two cases), and those who had no beneficial effect (eight patients). Several of the latter group died before an effective therapeutic program could be instituted.

TABLE III  
DIAGNOSTIC TESTS

| TEST                      | POSITIVE | NEGATIVE |
|---------------------------|----------|----------|
| Sputum cytology           | 7        | 11       |
| Bronchoscopy              | 2        | 8        |
| Scalene lymph node biopsy | 2        | 8        |

TABLE IV  
TISSUE DIAGNOSIS

| TYPE OF TISSUE              | NUMBER OF CASES |
|-----------------------------|-----------------|
| Epidermoid carcinoma        | 7               |
| Adenocarcinoma              | 4               |
| Undifferentiated carcinoma  | 7               |
| Carcinoma—no type specified | 1               |
| No tissue diagnosis made    | 2               |

Three patients treated with radical irradiation therapy without surgery obtained excellent pain relief, and two of these lived 4 and 7 months, respectively. The third, though still alive 18 months after treatment, has vertebral metastases.

### Discussion

Many previous authors<sup>1,2,4-6,9,11</sup> have noted the association of apical lung tumors and shoulder pain. However, only Onuigbo<sup>12</sup> stressed the frequency with which patients who have bronchogenic carcinoma in regions of the lung other than the apex present with shoulder pain. Although most of the lung tumors in this study were located in the periphery of the apical segment, approximately one-third were located elsewhere in the upper lobe.

Shoulder pain itself is a symptom which is often quite disabling and frequently requires medical attention.<sup>13</sup> The underlying causes are legion and range from osteoarthritis to angina pectoris. What is unique about the pain which develops in cases of carcinoma of the lung is that it is generally an intense burning or dull aching pain in and around the region of the scapula; the patients commonly complain of the pain radiating down the arm; and there is frequently an associated paresthesia.

This pain pattern is most commonly noted following compression of the lower cervical and upper thoracic nerve roots or brachial plexus. The compression may be secondary to direct involvement of the nerve in contiguous tumor growth across the adherent pleura or to perineural lymphatic metastases. The former mechanism is frequently the case in patients with peripheral apical tumors, the usual Pancoast tumor. The perineural lymphatic seeding, on the other hand, occurs by tumor spread

TABLE V  
TREATMENT

| TYPE OF TREATMENT                                                 | NUMBER OF CASES |
|-------------------------------------------------------------------|-----------------|
| Radiation therapy—radical                                         | 3               |
| Radiation therapy—palliative                                      | 5               |
| Radiation therapy—radical plus surgery—curative                   | 3               |
| Chemotherapy                                                      | 2               |
| Chemotherapy plus radiation therapy—palliative                    | 5               |
| Surgery followed by chemotherapy and radiation therapy—palliative | 1               |
| No specific therapy                                               | 2               |

to the pleura and thus to the lymphatic bed in the endothoracic fascia or by spread through the lymphatic channels draining the pulmonary parenchyma via the hilum and thence to the perineural lymphatics.

In the present series of cases, neural involvement by tumor occurred through both contiguous tumor growth and perineural metastases. As one would expect in such a series, there was a high incidence (thirteen cases) of hilar and mediastinal lymphadenopathy. This feature in and of itself illustrates how a non-apically located lung tumor may present with shoulder pain secondary to perineural metastases.

Additional, less common causes of shoulder-arm pain in lung cancer include bone metastases and ischemia from arterial involvement. Two cases in the present series had obvious humeral metastases.

Upon reviewing this study it is obvious that shoulder pain is a poor prognostic sign. The patients' survival from first symptom to death in the twenty cases who have succumbed averaged 10.7 months duration. Only one patient survived five years, not the one presently living, and none longer. When shoulder pain is due to tumor, the latter is probably unresectable. However, in some cases one cannot be certain of the origin of the shoulder pain; only at a later date, after performing an apparently complete resection, does one find that distant metastases had already occurred. The preoperative performance of scalene lymph node biopsies may hopefully reduce the percentage of such cases.

The outlook for patients with shoulder-arm pain secondary to bronchogenic carcinoma is somewhat brightened by several recent reports. In 1956, Chardack and MacCallum<sup>8</sup> described a patient with Pancoast syndrome who had an apparently complete surgical resection of the tumor followed by radical irradiation therapy. The patient survived 5 years and 10 months after operation, dying of bronchopneumonia and heart failure. At post-mortem examination no evidence of residual tumor was found.

Shaw, Paulson and Kee<sup>9</sup> reported in 1961 a series of eighteen patients with superior sulcus tumors treated by irradiation and subsequent resection. Groves<sup>5</sup> in 1962, reported on ten patients with the Pancoast syndrome treated by incomplete surgical resection followed by irradiation. The majority of the patients in both groups obtained significant palliation, and one or two "cures" were included in the series. Thus, the prognosis may not be as bleak as this present series seems to indicate.

The necessity for careful diagnostic study of all patients who come to the doctor's office complaining of shoulder pain is obvious. When a patient presents with pulmonary symptomatology in addi-

tion to shoulder pain, the realm of diagnostic possibilities is considerably reduced, and the physician's attention is focused on the chest. It is for the patient who only complains of shoulder pain that the physician's suspicion must include bronchogenic carcinoma, and X-rays should include an examination of the lung fields.

### Summary

A review of 150 cases of upper lobe bronchogenic carcinoma revealed 21 presenting with shoulder-arm pain (14 per cent). Four of these had centrally located upper lobe tumors lying near the hilar region of the lung and the remainder demonstrated peripheral lesions. The mechanism of production of shoulder pain and the prognostic significance are discussed. The necessity for early chest films is emphasized.

### Acknowledgment

Supported in part by a Public Health Service Fellowship (1-F2-HE-23,111-01) from the National Heart Institute.

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# FROM THE GENERAL MANAGER'S OFFICE

WILLIAM R. RICHARDS, M.D., *General Manager*

James G. Burch

*Director of Public Relations*

160 St. Ronan Street, New Haven, Conn.

Telephone 865 0587

Josephine P. Lindquist

*Assistant to General Manager*

## SUMMARY OF ACTIONS COUNCIL MEETING

Thursday, February 17, 1966

### I. Attendance

Present in addition to the Chairman, Dr. S. J. Martin, were: Drs. Cullen, Hess, Bradley, Goldberg, W. Martin, M. Caplan, Brandon, Gardner, Pitock, H. Caplan, Rogol, Grendon, Egan, Deming, Shepard, Nolan, Cramer, Fabro, Abbot, Petrie, Wilson and Roch. Also present were: Mrs. Lindquist and Dr. Richards. Absent were: Drs. Weise, Sr., Spitz, Palumbo, Ayres, Ciccarelli, Epstein and Hastings.

### II. Routine Business

#### Approval Of Minutes

As printed and distributed, it was VOTED to approve the minutes of the meeting of January 26, 1966.

#### Life Membership

It was VOTED to approve applications for Life Membership of the following eligible Active Members of the Society:

Charles M. Gratz, Greenwich (FCMA)  
William E. Hall, Meriden (NHCMA)  
Thomas D. Murphy, Manchester (HCMA)  
Frank E. Roth, Hartford (HCMA)  
Joseph Weiner, New Haven (NHCMA)

#### Election Of Student Member

It was VOTED to elect Mr. William F. Crowley, Jr., New Britain, who is attending the Tufts Medical School, to Student Membership in the Society.

#### Proposal—Advisory Committee On School Health

Acting on a proposal of this Committee (approved by the parent Committee on Public Health) to publish three school health newsletters a year as a supplement to the Journal, it was VOTED to commend the Advisory Committee for its initiative; to inform the Committee on the Council's opinion that such a newsletter should have a wider distribution than proposed (educators, physical education teachers, etc.); to suggest that the Committee seek liaison with the State Departments of Health and Education concerning cooperation in the proposed project and the possibility of coordinated distribution, and to defer

action on the proposal until the foregoing suggestions have been explored by the Committee.

#### Appointment—Joint Conference Committee With the Bar Association

It was VOTED to appoint John E. Darrow, New Britain, to membership on this Committee for the balance of the year, and to place his name in nomination for membership on the Committee for 1966-67.

#### Date Of Next Meeting

The next meeting was scheduled for Wednesday, March 23, 1966.

### III. Old, New And Special Business

#### Report—AMA National Conference On Federal Medical Assistance Programs

It was VOTED to accept, with commendation, the report on the proceedings of this Conference which was filed by Peter J. Scafarello, Hartford, and Isadore H. Friedberg, Newington, who attended as representatives of the Society. Concerning a recommendation of the report that a "task force" be appointed to deal with the Welfare Department "on a high plane" (especially with respect to the implementation of Title XIX of P. L. 89-97 in Connecticut), the Council expressed the opinion that the presently "augmented" Advisory Committee to the Commissioners of Welfare, Finance and Control should be able to carry out this purpose. The "augmentation" consists of the addition to the Advisory Committee of the CSMS Committee on Third Party Payments as well as representatives of the Council (the president, president-elect, the chairman, the general manager, etc.).

Subsequent to the acceptance of this report, several members of the Council reported on the proceedings of a conference between the augmented Advisory Committee and Commissioner Shapiro, which was held on February 10, 1966. At this conference, the Commissioner informed the CSMS representatives of his plans for implementing the expanded Kerr-Mills program and the other provisions of Title XIX, on and after July 1, and of his intention of seeking approval of his plan by the Secretary of HEW et al in the near future. Despite his acknowledgment that the plan had short-

comings (which he claimed would have to be tolerated until the 1967 session of the General Assembly), it was reported that the Commissioner was hopeful that the Society would lend its approval and support to the program as he had outlined it at the meeting.

Following a prolonged period of discussion, it was VOTED to inform Commissioner Shapiro by letter (with copies to the Secretary of HEW and appropriate undersecretaries) as follows: That, having received verbal reports on his proposed plan for a July 1st implementation of Title XIX of P.L. 89-97 in Connecticut from Council representatives who were present at the meeting with him and his staff on February 10, the Council is of the opinion that the plan, as reported, is unacceptable to the Society because: (a) It will not offer adequate, high quality, comprehensive medical care to its recipients, and (b), the proposed payment schedules for physicians' services will be substandard, and out of keeping with the Society's present policy concerning "usual and customary" reimbursement.

Further, that the Society believes all persons should receive high quality, comprehensive medical care, irrespective of their ability to pay for it as individuals, and that when any agency proposes to pay for such care on any person's behalf, the providers of services should be paid at their usual and customary rates. In conclusion, the Council wishes to urge the Commissioner not to seek HEW approval of the plan that he is now proposing, and to inform him that the Society, through its representatives and committees, will be glad to make formal, constructive recommendations concerning his present proposal if he will submit same to the Council in printed and detailed form.

#### **Resignation—Director Of Public Relations**

In a letter addressed to the General Manager, with a request that it be presented to the Council, Mr. James G. Burch, Director of Public Relations and Communications, informed the Council that "after twenty years of service for the Society, (he) regrets that (he) now finds it necessary, for personal reasons, to resign from (his position), effective April 1, 1966."

It was VOTED to accept Mr. Burch's resignation, with regret; to thank him for his many years of service with the Society; to assure him that his rights in the Pension Plan would be fully protected; and that his present salary would be continued through June 30, 1966.

Subsequently, it was VOTED to direct the Ad Hoc Committee on Staff Structure, in conjunction with the Chairman of the PR Division, to proceed forthwith to establish qualifications to be sought in a person or in persons to carry out an adequate public relations program for the Society, and to

then proceed, without delay, to select such person or persons to be recommended to the Council for employment.

#### **Report—Council Committee On Preliminary Study Of Nominations**

The Committee filed a complete slate of nominees for CSMS officers, committees, representatives, delegates, etc. for 1966, which, after several amendments, was VOTED to be the official slate of such nominees of the Council to be transmitted to the House of Delegates on April 26, 1966 for election. The bulk of the nominations will be published in the Delegate's Handbook for the Annual Meeting.

For the major offices, those nominated by the Council will be:

For President—Orvan W. Hess, New Haven  
For President-Elect—E. Tremain Bradley, Norwalk  
For Vice-President—Norman H. Gardner, East Hampton  
For Secretary—Waldo E. Martin, Milford  
For Treasurer—Isadore S. Goldberg, Torrington  
For Speaker of the House—Kenneth F. Brandon, Hartford  
For Vice-Speaker of the House—Henry Caplan, Yalesville  
For Councilor-at-Large—Charles Polivy, Hartford  
For AMA Delegate, January 1, 1967-December 31, 1968—Stuart P. Seigle, Hartford  
For Alternate AMA Delegate (same term)—J. Alfred Fabro, Torrington  
For AMA Delegate, January 1, 1967-December 31, 1968—Max Caplan, Meriden  
For Alternate Delegate (same term)—Morris P. Pitock, Bridgeport

#### **Motion Re Separate Billing By Hospital-Based Specialists**

Introduced by David A. Grendon, Councilor from LCMA, it was VOTED to adopt a motion as follows:

IT IS MOVED: That the Council authorize a letter to be sent to each county medical association, each city or regional medical society, and to the chief of staff of every hospital in Connecticut, informing them of the action taken by the CSMS House of Delegates on December 9, 1965, endorsing the principle of separate billing for their services by hospital-based specialists, and encouraging those associations, societies and medical staffs to take similar actions.

#### **Request—Connecticut General Life Insurance Company**

In a letter dated February 11, E. Stuart McCleary, M.D., of the Connecticut General Life Insurance Company, informs the Council that Connecticut General has been designated by the Social Security Administration (HEW) to be fiscal agent



(carrier) for Medicare's Part B in Connecticut, and requests that "one of (the Society's) standing committees be designated, or a new committee appointed, to meet with Company representatives on Medicare."

It was VOTED to request the President, Dr. Cullen, to appoint a special committee for this purpose, such committee to be made up of state officers, representatives of the Committee on Third Party Payments, the General Manager, and others that may be selected by the President.

#### **Nomination To The Hospital Planning Commission**

It was VOTED to approve the nomination of David A. Grendon, Sharon, as proposed by the Ad Hoc Nominating Committee (The President, the Chairman of the Council, and the Chairman of the Committee on Hospitals), and to forward Dr. Grendon's name to the President of the Hospital Planning Commission as the Society's nominee to replace Gaert S. Gudernatch, Sharon, who was originally nominated to represent medical practice on the Commission but was unable to serve. The other five nominees of the Society, who were subsequently elected to membership on the Commission, will be apprised of this action of the Council and urged to sponsor Dr. Grendon for election at the proper time.

#### **Resolution—Discrimination In Organized Medicine**

Introduced by Paul H. Laviets, New Haven, and suitably amended by the Council to carry out its intent, it was VOTED to adopt the following resolution and transmit same for adoption by the House of Delegates on April 26, 1966:

WHEREAS: Since 1939, resolutions have been presented to the House of Delegates of the American Medical Association stating that "membership in constituent state associations and component county or district societies shall not be denied on the basis of race, creed or color," therefore be it

RESOLVED: That the House of Delegates of the Connecticut State Medical Society go on record as approving fully the principle that membership in the American Medical Association of any constituent association shall be revoked if such constituent association shall allow any of its component societies to deny membership to any individual on the basis of race, creed or color, and be it further

RESOLVED: That the Society's Delegates to the American Medical Association introduce the foregoing resolution at the June, 1966 meeting of the AMA House of Delegates and work to secure its adoption by that body.

#### **Report—Committee On Third Party Payments**

When the CSMS Relative Value Schedule was adopted by the House of Delegates on April 27,

1965, one of the recommendations corollary to the Schedule was that: "All CSMS committees which are advisory to *governmental* third parties in the matter of payment schedules" should "be authorized not only to use the CSMS Relative Value Schedule as a guide (in their advisory functions), but also to *suggest* conversion (dollar) factors which they believe are appropriate in assisting the governmental third parties to develop schedules that conform to the principle of parity of payments to physicians in the State, in line with 'usual and customary' charges".

Subsequently, the Council requested the Committee on Third Party Payments to consult with the governing bodies of all CSMS sections and allied groups that participated in the original Relative Value Study for the purpose of obtaining "suggestions" from these sections and groups as to what dollar conversion factors applied to the listed RV units in the major divisions of the Schedule (Medicine, Surgery, Anesthesiology, Radiology, Pathology) would develop payment schedules in keeping with the intent of the House of Delegates (stated in the preceding paragraph).

The Committee on Third Party Payments, having completed the task assigned to it, filed a report with the Council at this meeting, which report asked for Council approval of the dollar conversion factors suggested for four major divisions (Pathology asked to be excluded at this time), and recommended that CSMS committees advising governmental third parties be authorized to use those factors in conjunction with the CSMS Relative Value Schedule for the purposes stipulated by the House of Delegates and with a view to obtaining "reasonable conformance" by the respective governmental third parties with the RV Schedule and the suggested conversion factors.

Discussion of this report took up approximately two hours of the time of the meeting, and at least five motions concerning its reception, acceptance, approval, etc. were introduced but defeated by majority vote. The principal arguments advanced against its acceptance (and implied implementation) were that (a) the use of conversion factors with the RVS (even in the limited area prescribed) would establish a statewide "fixed fee schedule," which is contrary to CSMS policy, and (b) that the fees structure derived from the conversions factors suggested would be neither "usual" nor "customary" in some parts of the State, especially where normal charges are known to be substantially lower than those in other parts of the State. The principal arguments advanced for adopting the report and its recommendations were that (a) advisory committees dealing with governmental third parties need to have some guidelines as to appropriate conversion factors, and (b) that the impending

implementation of Medicare's Part B makes it even more imperative to have such guidelines. In the end, two actions were taken on the report as follows:

(1) It was VOTED to accept the report, with commendation, but to recommend that the suggested conversion factors *not* be used to set up any payment schedules at this time.

(2) It was VOTED that the Council commit itself to the concept of "usual and customary fees," as determined at local level, and recommend that the Relative Value Schedule and other available means (aids) be used by all concerned to implement this concept.

**Request—UConn Health Center (Medical-Dental School)**

The Council was notified that the new UConn Medical-Dental School is seeking to build up its medical library, and is especially interested in establishing "exchange" arrangements with organizations and agencies publishing scientific journals. To this end, Mr. Sam W. Hitt, Librarian, requests that the School be given up to 50 copies of *CONNECTICUT MEDICINE* to be used as its "exchange" publication for the purpose stated. It was VOTED to approve this request, being hopeful that the Society would receive acknowledgement for same, with the understanding that it would be continued for up to three years, if necessary.

**Advisory Council To Connecticut's "Regional Medical Program"**

Orvan W. Hess, New Haven, informed the Council that he (as next year's president) had been invited by the Yale and UConn Medical Schools to serve on the Advisory Council of the regional medical program (DeBakey legislation) which is being planned by the two schools. Dr. Hess explained that he would be serving as a representative of the Society.

Expressing approval that Dr. Hess had been selected by the deans of the respective medical schools, the Council VOTED to reaffirm its previous position that medical practice should have substantial representation in programs of this nature (the Hospital Planning Commission, etc.) and its previous offer to furnish same (via letters from Dr. Cullen to the medical school deans); also, to direct the Committee on Cooperation with the Yale School of Medicine to offer its services as a participant in the planning phase for implementing P.L. 89-97 in Connecticut.

**Commendation—Chairman, Committee On Hospitals**

Having learned from the report of the Committee on Preliminary Study of Nominations that Leopold M. Trifari, Hamden, must decline to serve again as Chairman of the Committee on Hospitals, and, in fact, with any committees of the Society for

the next year or two, it was VOTED unanimously to commend Dr. Trifari for his many years of competent, dedicated and productive service with the Committee on Hospitals both as a member and as its chairman.

**N.B.:** *The foregoing is a summary of the proceedings and actions of the Council on February 17, 1966. Detailed minutes of the meeting are on file at 160 St. Ronan Street, New Haven, for perusal by any interested member of the Society.*

**PLACEMENT WANTED**

**OBS-GYN**—Military and Board requirements completed, subspecialty training in gynecological cancer, seeks opportunity for solo, partnership or association within traveling distance of New York City beginning July 1966.

**PATHOLOGIST**—Board certified in Clinical Pathology and eligible in Anatomic Pathology and Internal Medicine. Connecticut license, degree in Public Health. Wishes to locate in Connecticut in a situation that would allow full use of diversified training.

**PEDIATRICIAN**—29 years of age, presently completing military obligations. Would like to associate with another pediatrician within traveling distance of New York. Available July 1, 1966.

**SURGEON**—35 years of age, board eligible, Connecticut license. Military obligations completed, would like either an association or join a group practice. Available as of July, 1966.

**SURGEON**—34 years of age, Board eligible, Connecticut license. Military obligations completed, would like to associate with another surgeon or become part of a group practice. Available July 1, 1966.

**UROLOGIST** — Board eligible, Connecticut license. 34 years of age, with military obligations fulfilled. Available July, 1966 and would like to enter into an association or solo practice.

**UROLOGIST**—31 years of age, military obligations completed. Board eligible. Connecticut license. Would like to enter group practice as of July 1, 1966.

**G.P.**—39 years of age, ineligible for draft, would like to practice with either a group or an associate as of June, 1966. Presently in England and will be coming to this country in June. Completed military obligations in British Merchant Navy.

**PLACEMENT OPPORTUNITIES**

**WANTED**—House Physician—diversified duties in accredited, voluntary hospital. Connecticut license required, no weekends. \$15,000 yearly. Please reply to: P.O. Box 638, Bridgeport, Connecticut 06601.



**INTERNIST**—Board eligible or certified Internist with sub-specialty training in Gastroenterology to join a multi-specialty group in New Britain. Eligibility for, or Connecticut license required.

**PATHOLOGIST**—Full or half-time to direct the clinical laboratory in a 2300 bed mental hospital. Ample opportunity for teaching and research available. Well equipped and fully staffed laboratory. Emphasis on neuropathology. Board certified or eligible Pathologist preferred. Salary range: \$14,740-\$19,100. Fringe benefits: 3 weeks' paid vacation, 3 weeks' paid sick leave, 11 paid holidays, free Blue Cross, CMS and Major Medical Insurance. Contact John F. Lowney, Jr., M.D., Superintendent, Connecticut Valley Hospital, Middletown, Conn.

**CLINICAL DIRECTOR** to develop program in psychiatric hospital with emphasis on psychosomatic medicine. Opportunity for experience in employees' health clinic, workmen's compensation clinic and psychopharmacologic drug research. Will direct department already staffed by seven doctors. EEG, EKG, Ophthalmology, Radiology Departments already fully equipped and staffed. Consultants available in every medical and psychiatric specialty. Opportunity for program to be affiliated with Yale, Wesleyan, UConn and local general hospitals. All particulars should be sent in first letter, including references. Apply: John F. Lowney, Jr., M.D., Superintendent, Connecticut Valley Hospital, Box 351, Middletown, Conn.

**CLINICAL OPENINGS** for physician-internist or general medical background—to practice in association with other physicians; merit system, attractive salary and retirement benefits with excellent sick leave, vacation and insurance benefits. WRITE: State Health Department, 79 Elm Street—Room 301, Hartford, Connecticut 06115. **EQUAL OPPORTUNITY EMPLOYER.**

**WANTED, COLLEGE PHYSICIAN** — for women's college, 1400 students. Out-patient and in-patient services, with nursing staff and laboratory. Full-time or part-time. Write: Mary N. Hall, M.D., Connecticut College, New London, Connecticut.

**INTERNIST**—Board certified or eligible Internist wanted to take over fully established practice and office of physician who is leaving Connecticut shortly. Located in Glastonbury, Connecticut, just a few minutes from Hartford Hospital.

**PATHOLOGIST**—500 bed, general, medical and surgical hospital for male Connecticut resident veterans. Salary range \$14,740 to \$19,000. Excellent fringe benefits, including group life insurance and Major Medical Insurance and Social Security. Housing accommodations available at low-cost maintenance. For further information, contact: Person-

nel Office, Veterans Home and Hospital, Rocky Hill, Connecticut.

**DISTRICT HEALTH DIRECTOR** for Weston/Westport, Conn. Required M.D. plus degree in Public Health or equivalent experience. Salary range \$18,500 to \$22,500, to be negotiated, depending upon qualifications. Start: July, 1966. Send resume to: Clifford Mills, M.D., Chairman; Weston-Westport Health District; c/o Health Department; Westport, Conn. 06880.

**INTERNIST OR G.P.** for a three-man group. Have regularly visiting specialist consultant staff, modern clinic facilities, scheduled training and vacation periods. Starting net income \$15,000 to \$18,000 depending on qualifications. Partnership in one year.

**ANYONE INTERESTED IN THE ABOVE IS ASKED TO CONTACT THE GENERAL MANAGER'S OFFICE, 160 ST. RONAN STREET, NEW HAVEN, CONNECTICUT 06511.**

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#### **GAYLORD DAY—GAYLORD HOSPITAL AND SANATORIUM**

**Wallingford, Connecticut**

**May 25, 1966 — 2:00-6:00 P.M.**

Please save the above afternoon to join us for the following presentations:

Newer Developments in Bracing (Orthotics)

Hans R. Lehnies, Chief, Orthotics, New York University Medical Center, Institute of Physical Medicine and Rehabilitation.

Low Back Pain, Treatment including Bracing.

Rene Cailliet, M.D., Associate Clinical Professor, University of Southern California, School of Medicine, Department of Physical Medicine and Rehabilitation.

Cerebral Palsy, Birth Defects —

Treatment including Bracing and Surgical Measures.

Leon M. Kruger, M.D., Orthopedic Surgeon, Shriner's Hospital for Crippled Children, Springfield, Massachusetts.

Buffet dinner courtesy of Gaylord Hospital will be served at 6:30 p.m.

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#### **VENEREAL DISEASE CONTROL LECTURES**

**April 14, 1966 — 5:00 P.M.**

The Yale University School of Public Health in cooperation with the New Haven Health Department will present a major lecture on Venereal Disease Control on April 14, 1966, at 5:00 P.M. in Harkness Auditorium at the Yale University Medical School. Guest speaker for this lecture will be Dr. Eugene J. Gillespie, Deputy Chief, Venereal Disease Branch, Communicable Disease Center, Atlanta, Georgia. Doctor Gillespie will address himself to the problems of Venereal Disease Control which have particular application to the physician in private practice, such as diagnosis and treatment and new advances in research.

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## AROUND THE STATE

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### Yale Names Chair For Dr. Long

With an anonymous gift of \$600,000, Yale University will establish a new chair in honor of one of the university's leading scientists, former dean of the medical school Dr. C. N. Hugh Long.

In his announcement Yale President Kingman Brewster Jr. said the professorship will be in the Yale School of Medicine and has been specifically endowed for studies in endocrinology and metabolic diseases, such as diabetes and hypertension. The first incumbent will be appointed shortly.

The professorship is the 200th endowed chair in Yale's history. The first endowed professorship was created in 1746 just 45 years after Yale's founding.

Dr. Long, 65, a member of the Yale faculty since 1936, is currently Sterling Professor of Physiology. He served as dean of the Yale medical school from 1947 to 1952 and has been at various times chairman of three departments at the school.

Dr. Vernon W. Lippard, dean of the Yale School of Medicine and Dr. Long's successor in this post, pointed out that "the establishment of this professorship will add new strength to our instruction are research in the important field of endocrinology. It is a most appropriate tribute to Dr. Long, one of the world's leading scientists in this field."

Dr. Long is noted for his major contributions in biochemistry and physiology. Among his outstanding research projects are his work on the importance of various endocrine glands—particularly the adrenal—in diabetes; his investigations into carbohydrate metabolism; and his studies that have advanced the physiological theory of muscle activity.

A native of Nettleton, England, Dr. Long was born in 1901. He received his bachelor, master, and doctor in science degrees from the University of Manchester, and the doctor of medicine and master of surgery degrees from McGill University in Canada.

He came to the United States in 1932 as director of the George S. Cox Medical Research Institute and assistant professor of medicine at the University of Pennsylvania.

He joined the Yale faculty in 1936 as professor of physiological chemistry and chairman of Yale Laboratory of Physiological Chemistry. He was named Sterling Professor of Physiological Chemistry in 1938.

When he stepped down in 1952 as dean of the Yale Medical School, he became Sterling Professor

of Physiology and chairman of that department. He relinquished the chairmanship in 1964.

Dr. Long has served on many high-ranking committees of governmental and private agencies. From 1959 to 1961 he was chairman of the Divisional Committee for Biological and Medical Sciences of the National Science Foundation (NSF). Since 1960 he has been a consultant to the President's Scientific Advisory Committee, and has been also a consultant to the surgeon general of the Army Medical Corps (1947-48) and the U.S. Public Health Service (1945-1949 and 1958-1959).

In 1965 Dr. Long served as a member of a mission on medical education to Egypt, sponsored by the Agency for International Development and the Assoc. of American Medical Colleges. He also was part of a joint mission conducted by the Unitarian Service Committee and Department of the Army in 1950 to help reorganize medical education in Japan.

### New Haven County

*Outgoing remarks by Dr. Joseph Weiner, President of the New Haven Medical Association*

These are changing times. We must keep abreast with the rapid changes taking place in medicine and the changing pattern of medical care.

Article II of our Constitution states our purposes, and I quote:

"To devise and carry into effect measures for the scientific and educational advancement of the members and to promote good understanding and harmonious relationship with each other and the community."

Our meetings and our colleagues have been oriented towards scientific and educational training. But what have we done to establish a good understanding and harmonious relationship with the community? When we speak of the community we do not mean only New Haven, but the public in general. How well have we succeeded in bringing to the public the meaning of medicine and our role in Society? Have we given thought to what the people are thinking about us? We are acting our usual role in giving personal service to an individual patient, but hardly aware of the changes taking place in the Bio-Medical sciences as they relate to our social role.

Practicing physicians were for a long time uncertain whether such changes were occurring and were either denying or resisting them. Now the changes are fully upon us. Medicare is a perfect example of



our resisting a change and we are not yet quite prepared to learn its lesson and what we need do about it. We are now at a stage when we must redefine the core of professional activity. What the practice of medicine really is and what is the central medical task. The fundamental task, the care of the patient is no longer a simple matter. There is continual evolution in personal medical care. There are two million people employed in the health services and 225,000 physicians, in addition the public has become a third party to the contract between physician and patient. There are changing arrangements for providing care, such as teaching institutions, medical hospital centers, group practices and specialists of all kinds. This is the result of rapid evolution of Bio-Medical science. The American Medical Association last October, dedicated a new Institute for Bio-Medical Research in recognition of the importance of this science.

There are changing patterns of illness. Infectious diseases have declined. There is much more degenerative diseases and malignancy to be recognized and treated in the early and later stages.

There are changing directions which graduate physicians are taking toward careers as specialists and medical scientists and away from general practice.

Then there are changing ways of paying for this increased complexity of medical care. If we are to satisfy the requirements of our constitution, we must begin to pay more attention to our social role. To what the public expects of us and how we should face up to, and take the leadership in, the administration of Public Laws dealing with medical care.

The new era in medicine requires a doctor who knows what is going on in Bio-Medical advances and who also knows how to take his rightful place in the administration of health laws, so that medical care will not suffer and the patient will benefit. If we do this the physician is bound to gain too.

In concluding this report of my tenure, I wish to express my deep gratitude for your confidence in electing me your President for the past year. I have exerted my best efforts to serve you. It was a rewarding experience.

**New Haven County  
Meeting of the Board of Governors  
New Haven County Medical Association  
February 24, 1966**

As usual, a full attendance of the members of the Board of Governors was recorded. Doctors William Richards, Orvan Hess, Clyde Deming and A. J. Mendillo were our guest members.

Much of the meeting dealt with Title XIX of the Medicare Bill. Our Councilor, Dr. Frank Abbot,

reported that State Welfare Commissioner Bernard Shapiro desires to further implement the Expanded Kerr-Mills program on and after July 1, 1966. He admits his plans will have certain short-comings until the 1967 Session of the Connecticut General Assembly.

After considerable discussion of this feature of the Councilor's Report, and other matters pertaining to Title XIX, Dr. Max Caplan moved the following telegram be sent to Commissioner of State Welfare Shapiro:

"The New Haven County Medical Association is unalterably and irrevocably opposed to sub-standard medical treatment or sub-standard medical fees for the treatment of any patients in our State including those under Title XIX."

Respectfully submitted,  
H. A. LEVIN, M.D., *Clerk*

**Dr. Celentano Appointed**

Dr. Luca E. H. Celentano of New Haven, has been appointed to the Governor's Fitness Commission. He succeeds Dr. Allan J. Ryan, formerly of Meriden, who heads the department of sports medicine at the University of Wisconsin.

Dr. Celentano is past president of the New Haven County Medical Association and the New Haven Medical Association. He is a Delegate to the Connecticut State Medical Society and chairman of the Public Relations Division.

**Side Effects—True or False?**

The (FDA) adverse reaction program is off to a fair start and should get better, but concentration on side effects has put too much information into the hands of the laity and the uninformed, who tend to misinterpret. As a consequence, more side effects are being reported now that aren't really side effects, but rather the imaginations of those who got their hands on medical advertising or package inserts. It is the duty of the manufacturers to provide all the information to the physician about the drugs they make. All side effects should be clearly spelled out for him, but they should not be emphasized over and above the therapeutic activity.—Robert W. Ballard, M.D., in *Food Drug Cosmetic Law Journal*. (21:31), January 1966.

**THE HAVEN, INC.**  
**Nursing Home for**  
**Chronic and Convalescent Cases**  
**ABINGTON, CONN.**

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mate include: skin rash, nonthrombocytopenic purpura with petechiae, ecchymoses, peripheral edema, fever and transient leukopenia; also, very rarely, fainting spells, angioneurotic edema, bronchial spasm, hypotensive crisis, anuria, stomatitis, proctitis and anaphylaxis. Other serious effects have occurred after concomitant administration of meprobamate and other drugs. Massive overdosage may produce grave effects.

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## In Memoriam

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**Claiborn, Louie N.**—New Haven; Washington University School of Medicine, 1928. Dr. Claiborn had been associated with the Yale-New Haven Hospital since 1929 and was associate clinical professor of plastic surgery in the Yale School of Medicine, as well as surgical consultant in the Department of University Health. He served on the staff of several hospitals, as consultant in surgery at Middlesex Hospital, Middletown, Griffin Hospital, Derby, Fairfield State Hospital, Newtown, and Veterans Administration Hospitals in Newington and West Haven. He was president of the New England Society of Plastic and Reconstructive Surgery. He was a member of the New Haven County Medical Association, the Connecticut State Medical Society, the American Medical Association, the American College of Surgeons, the Society of University Surgeons, the New England Surgical Society, the American Society of Plastic and Reconstructive Surgery, the Connecticut Society of American Board Surgeons, the New York Regional Society of Plastic and Reconstructive Surgery, and a fellow in the American College of Surgeons. Dr. Claiborn died February 16, at the age of 62.

**Knight, Harry C.**—Middletown; Tulane University School of Medicine, 1933. Dr. Knight was a well known urologist in the Middletown area for many years. During World War II, Dr. Knight was associated with the United State Public Health Service. He was a member of the American Urology Association, the New England Section of the American Urology Association, the American Geriatrics Association, the American Medical Association, the Connecticut State Medical Society, and the Middlesex County Medical Association. He was a fellow of the American College of Surgeons. Dr. Knight was senior attending urologist at the Middlesex Memorial Hospital, Middletown, and urology consultant at the Middletown State Hospital and the Veterans' Memorial Hospital in Rocky Hill. He was a member of the courtesy staff at the Meriden Hospital. Dr. Knight died March 12, at the age of 60.

**Lankin, Joseph J.**—Hartford; Harvard Medical School, 1937. Dr. Lankin was a noted specialist in arthritic and rheumatic diseases. He had served as president of the Arthritis and Rheumatism Foun-

dation. He had appeared on television, radio, and in person to speak about his field of rheumatism. He also wrote numerous papers on the subject. He was a member of the Hartford County Medical Association, the Connecticut State Medical Society, and the American Medical Association. Dr. Lankin died March 8, at the age of 54.

**Reidy, David D.**—Hartford; Columbia College of Physicians and Surgeons, 1927. Dr. Reidy was a well-known urologist in Hartford for over 20 years. He was former chief of the medical staff at St. Francis Hospital. He was assistant urologist at Manchester Memorial Hospital and was consulting physician and surgeon at Litchfield County Hospital, as well as being chief urologist at St. Francis Hospital. He had been director of the St. Francis Hospital Association. He was a diplomate of the American Board of Urology and a member of the New England Section of the American Urology Society and pioneered in the use of the artificial kidney machine. He was a member of the Hartford County Medical Association, the Connecticut State Medical Society, and the American Medical Association. Dr. Reidy died March 8, at the age of 64.

**Segnalla, Ernest**—Hamden; Yale University School of Medicine, 1912. Dr. Segnalla was a general practitioner in the New Haven area for more than 50 years. He was a member of the New Haven County Medical Association, the Connecticut State Medical Society, and the American Medical Association. Dr. Segnalla died February 16, at the age of 77.

**Smith, Norman N.**—New Haven; Yale University School of Medicine, 1924. Dr. Smith was an eye, ear, nose and throat specialist in New Haven for over 20 years. He was a member of the staffs of both the Hospital of St. Raphael and the Yale-New Haven Hospital. He was a past president of the American Otorhinologic Society, a diplomate of the American Board of Otolaryngology, a member of the Society for the Advancement of Plastic and Reconstructive Surgery, the New Haven County Medical Association, the Connecticut State Medical Society, the American Medical Association, and a fellow of the International College of Surgeons. Dr. Smith died March 12, at the age of 65.



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## Letters To The Editor

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### To The Editor:

I wish to comment on Dr. Paul N. Graffagnino's article "The Brain-Damaged Child: A Misconception?" which appeared in the February 1966 issue of our *Journal*. I heartily endorse his efforts to rid us of this atrocious term. However, I observe that the tendency to develop unscientific notions about the disorder does "extend beyond the general public into professional ranks." Dr. Graffagnino states "the purpose of this paper is to define and describe this clinical entity, discuss its etiology, outline diagnostic procedures, suggest a program for treatment of the syndrome, and finally to discuss some of the misconceptions that interfere with successful management."

He alleges that the brain-damaged child manifests the cardinal symptoms of "impulsiveness, distractibility and restlessness." These behavioral signs occur in a large number of disorders, organic and functional alike. It is difficult to think of a clinical entity when a child is referred for such generalized "symptoms" as "learning defects," "unpredictable behavior," "extreme emotional lability," "social incompetence," etc.

When we look for an etiology, Dr. Graffagnino admits that "so far it has not been possible to correlate the clinical symptomatology and the structural damage to the brain in a scientifically valid way." Thus we have neither a clinical entity nor an etiology.

Here his use of the term "diagnosis" is disputable since he states that "no one physician or other specialist is qualified to make a diagnosis of brain damage." A group of equivocal findings—no matter how many and by whom—remains only a group of equivocal findings and not a medical entity. Without a natural history, a causal agent, particular symptoms, positive clinical signs and tests, what is the specialist trying to diagnose?

It is understandable then that the "Treatment Program" offered by Dr. Graffagnino is a broad, non-specific one. With children I would caution the use of diphenylhydantoin sodium and dextroamphetamine sulfate because of the possibility of psychomimetic and paradoxical effects respectively.

His discussion of the far reaching stigma of this unjustified label is excellent. It is because of this stigma that the burden of solid proof must rest squarely on the shoulders of any physician who would tell parents that their child's brain is damaged. It should be kept high in the forebrains and hearts of all of us who try to help children. The substitution of other terms such as "organic factor," primary brain dysfunction, etc., are satisfactory although his term "component of brain-damage" would be as misleading as the original label. We must remember that we may uncover findings to indicate a functional disturbance within the brain, but unless we are examining the brain tissue itself, I do not see how we can conclude that it is damaged.

In summary I find that Dr. Graffagnino did not "define and describe this clinical entity" because he could not. It does not exist as a disease entity. It has neither specific symptoms, etiology, diagnosis, nor specific treatment. If after earnest

efforts we cannot now resolve this real, gray area to black or white, let us not crown our ignorance by calling gray a new medical illness. Better to practice forbearance, share the anxieties of vagueness and recriminations of uncertainty in this area than allow it to pass on to others much less able to endure it.

WILLARD GOLD, M.D.  
Medical Director,  
Child Guidance Clinic  
for Central Connecticut, Inc.  
Meriden, Conn.

ED. NOTE: *This letter was submitted to Dr. Graffagnino who makes the following reply.*

### To The Editor:

Dr. Gold's comments seem to me to emphasize two major points: first, that the term "brain damaged child" is an unfortunate one and second, that no such "disease entity" exists. With both of these I agree. Unfortunately both Dr. Gold and I are faced with an accomplished fact: the use of the term "brain damage" has such widespread acceptance in professional and lay circles alike that I do not share his implied optimism that anything he or I might do would materially help to rid us of the term. The purpose of my article was to bring to the attention of medical readers current information available on a concept which is being both used and abused.

It seems to me that the best we can do is to understand what the investigators are talking about when they use the term. It is necessary that the physician arm himself with such basic knowledge for those times when parents come to him asking about "brain damage" or telling him they believe their child to be "brain-damaged" from something they have been told by an informed neighbor or from what they have read in a "professional" column in the popular press. (Even now the term seems to be going somewhat out of fashion in favor of the "perceptually handicapped child," an equally unfortunate global term which also ignores the rest of the child's personality and life adjustment.)

While agreeing with Dr. Gold that the clinical phenomena should not be called a "disease entity," I would re-emphasize that we are nevertheless dealing with a "clinical entity" (i.e. "the organic factor") which can often be identified as a separate component in the total clinical picture of certain children with behavioral, learning or emotional disturbances. Whereas undeniably the etiology is unverifiable or unknown, it is my opinion that the symptoms, natural history, diagnostic approaches and treatment programs (including the various medications) are more soundly established than Dr. Gold seems to imply. True, at the end we are still left with a "gray area" disorder.

With regard to Dr. Gold's last point, I would comment that even though for intra-professional purposes one phrase or another may be used to facilitate our discussions and to further our understanding, one can only assume that a physician will not "pass on to others" (namely to patients

and their families) any term which would add to, rather than alleviate, their suffering.

PAUL N. GRAEFAGNINO, M.D.  
 Director, Children's Clinic,  
 The Institute of Living,  
 Hartford, Conn.

### To The Editor:

As the junior author of an article entitled "Management of Shoulder Injuries in Sport" which appeared in the CONNECTICUT MEDICINE Vol. 29 #10, pp. 723, October 1965 issue, I would like to make a few additional comments and corrections in regards to my feelings on treatment of complete acromio-clavicular joint dislocations.

My experience in treatment of this injury differs somewhat from the senior author. I personally feel that if done with a particular technique and with careful post-operative care, wire fixation treatment of this injury affords very satisfactory results. A report of 51 cases, many of which were treated with the crossed threaded wire technique, has been published by me and Capt. William Stryker in the *Journal of the American Medical Association*, Vol. 192, pp. 689-692, May 24, 1965. In this latter report, it was the feeling of the authors that a two threaded pin technique together with a repair of the fascial and ligamentus structure superior to the joint without coraco-clavicular fixation gave a very satisfactory result. It was the conclusion of this study that this technique was far superior to the non-operative measures and to the more extensive surgical procedures.

Bennington, Vermont.

Sincerely,

DUDLEY M. BAKER, M.D.

Bennington, Vermont

### To the Editor:

#### Podiatric Services In A Mental Hospital

We found certain individuals at Fairfield Hills Hospital partially disabled with advanced foot ailments. There were a multitude of over-developed, malformed, discolored, malodorous mycotic nails, large callosities and plantar corns, multiple corns disfiguring all toes, bunions of varying dimensions, overlapping toes, and extensive dermatophytoses.

Shoe fitting problems accounted for some of the foot ailments.

From March 1964 to March 1965 a total of 671 patients were seen for the first time in the Podiatry clinics plus 397 retreated.

An examination of the following summary indicates the variety of foot cases treated during this period.

|                                |       |     |
|--------------------------------|-------|-----|
| TOTAL PATIENTS TREATED         | 671   |     |
| TOTAL RETREATMENT              | 397   |     |
| Conditions Treated             | Women | Men |
| Onychocryptosis (Ingrown nail) | 20    | 20  |
| Inverted nails                 | 2     | 1   |
| Onychia and/or paronychia      | 3     | 6   |
| Club nails                     | 33    | 15  |
| Over-developed nails           | 80    |     |
| Mycotic nails                  | 32    | 4   |
| Corns                          | 85    | 62  |
| Callosities                    | 37    | 225 |
| Hyperidrosis                   | 6     | 36  |
| Anhidrosis                     | 4     | 7   |

|                                            |    |    |
|--------------------------------------------|----|----|
| Phytoses                                   | 10 | 12 |
| Fissures                                   | 12 |    |
| Tailor Bunions                             | 10 |    |
| Bunions                                    | 40 | 5  |
| Warts                                      | 4  | 58 |
| Hammer Toes                                | 5  | 24 |
| Over-lapping toes                          | 15 |    |
| Pes Cavus                                  | 8  | 2  |
| Pes Planus                                 | 6  |    |
| Exostosis (1st joint)                      | 3  |    |
| Depressed Metatarsals                      | 25 |    |
| Other Lesions (including Diabetic lesions) | 17 | 11 |
| Diabetics                                  |    | 46 |
| Circulatory Deficiency                     |    | 7  |
| Shoe Weight Dispersing Appliances          |    | 21 |

MICHAEL SIMKO, D.S.C.

JOSEPH STARR, Pod.D., A.A.C.F.S.

Bridgeport, Connecticut.

*Letters to the Editor are welcome and will be published for informative and educational purposes as space permits. As with other material which is submitted for publication, all letters will be subject to the usual editing. Address all correspondence to: THE EDITOR, CONNECTICUT MEDICINE, 160 St. Ronan Street, New Haven, Connecticut, 06511.*

## Special Notices

### HARTFORD HOSPITAL

#### SATURDAY MORNING 11 O'CLOCK GUEST SPEAKERS

April 2 to June 16, 1966

April 2—Thomas T. Amatrudo, M.D., Asst. Professor of Medicine, Yale

Subject: "Endocrine Mysteries"

April 9—Sydney Gellis, M.D., Professor of Pediatrics, Tufts

Subject: "Disaccharide Malabsorption Syndrome"

April 16—Allen Pierce, M.D., Asst. Professor of Medicine, Southwestern, Texas

Subject: "Sleep and Respiratory Acidosis"

April 23—Psychiatry Symposium—11:00 A.M. Hartford Hospital Amphitheater James Johnson, M.D., Chairman

April 30—Ralph D. Alley, M.D., Assoc. Professor of Thoracic Surgery, Albany

Subject: "Cardiac Aneurysm: Surgical Treatment"

May 7—Thomas N. Hepburn Memorial Lecture: Ward Soames, M.D., Chief of Urology, Millard Fillmore Hospital, Buffalo, New York

Subject: "Cryogenic Prostatectomy"

May 14—John H. Schilling, M.D., Professor of Surgery, University of Oklahoma

Subject: "The Pancreas—Surgical Problems"

May 21—George W. Mitchell, Jr., M.D., Professor of Obstetrics and Gynecology, Tufts

Subject: 10:00 A.M. "Conception Control"

11:00 A.M. "Gynecology Cancer Chemotherapy"

June 16—Hartford Hospital House Staff Graduation



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## WOMAN'S AUXILIARY COUNTY MEETINGS

Fairfield—Lower Fairfield County—Luncheon Meeting at the Red Coach Inn, Darien on March 31st, at 12:30.

Hartford—Annual Meeting, April 19th, at the Shuttle Meadow Country Club, New Britain.

Litchfield—Annual Meeting in June.

New Haven—Annual Meeting April 11th.

New London—Annual Meeting May 3rd, at the Yankee Motor Inn, New London.

Windham—Annual Meeting—Thursday, 21st of April.

Middlesex—Annual Meeting—April 13th.

National Convention—Chicago, 43rd annual convention of the Woman's Auxiliary to the AMA—June 26 to 30. Headquarters for the Convention will be the Drake Hotel on Chicago's lakefront.

*Sunday*, June 26—Reception from 6:00 to 8:00 P.M. honoring the auxiliary's president and president-elect.

*Monday*, June 27—Guest Day Luncheon to which representatives of more than 40 national women's organizations will be invited.

*Tuesday*, June 28—James Z. Appel, M.D., president of the American Medical Association, will speak at the Tuesday Luncheon honoring past presidents of the Auxiliary. Voting for the 1967 nominating committee will take place on Tuesday afternoon and national officers for 1966-67 will be elected and installed on Wednesday morning.

Teenage headquarters will be the Hotel Knickerbocker, across the street from the Drake Hotel. Gulliver's Trails, Inc., will plan the teenage program under the supervision of the auxiliary convention committee.

Last fall, Mrs. Dewey Katz, the only woman on an eight man committee was elected co-chairman of the Air Pollution Study committee of the Capitol Region Planning Agency. She has been the city of Hartford's only woman representative to the Agency since its inception seven years ago; and has served on the Publicity and the Land Use Committees in the past.

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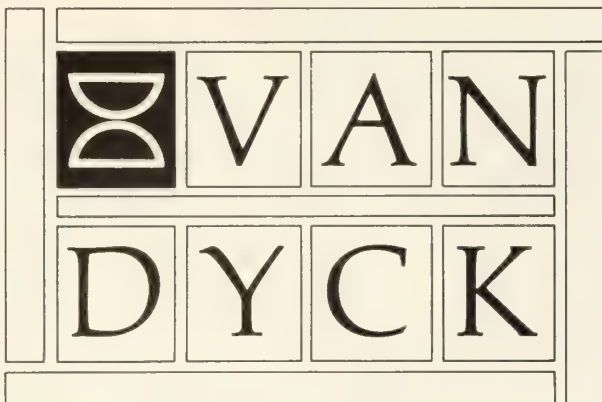
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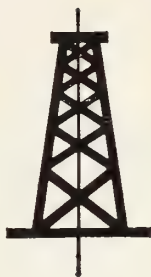
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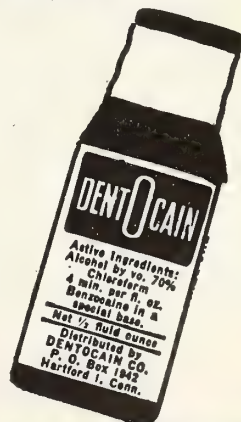
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## 1966 MEETINGS

**April 7** — ANNUAL MEETING of the New London County Medical Association, to be held at the Lighthouse Inn, New London. There will be a social hour at 5:30 P.M., dinner at 6:30 P.M. and the business meeting will begin at 8:00 P.M. with no speaker planned.

**April 12** — ANNUAL MEETING of Fairfield County Medical Association, to be held at the Stratfield Motor Inn, Bridgeport, Connecticut. The business session will begin at 4:30 P.M. with a social hour and dinner following.

**April 12** — ANNUAL MEETING of the Litchfield County Medical Association, to be held at the White Hart Inn, Salisbury, Connecticut. Business meeting at 5:30 P.M. with Dinner at 7:30 P.M.

**April 13** — ANNUAL MEETING of the Hartford County Medical Association to be held at the Statler-Hilton in Hartford. The business meeting will begin at 5:00 P.M. with the main speaker being Dr. Ernest Howard, Executive Vice-President of the American Medical Association. Dinner will follow at 7:00 P.M.

**April 14** — ANNUAL MEETING of the Middlesex County Medical Association to be held at the Commodore McDonough Inn in Middletown, Connecticut. The business meeting will begin at 4:30 P.M.

**April 19** — ANNUAL MEETING of the Tolland County Medical Association to be held at the Old Homestead Inn, Somers, Connecticut. Dr. Ernest N. Boettcher will be the speaker for the evening. His topic will be "Tooling Up For Medicare." Business Meeting: 6:30 P.M.

**April 21** — ANNUAL MEETING of the Windham County Medical Association to be held at the Vernon Stiles Inn, Thompson, Connecticut. The business meeting will begin at 5:30 P.M. with cocktails and dinner to follow at 7:00 P.M.

**April 26-28** — 174th ANNUAL MEETING of the Connecticut State Medical Society to be held at the Statler-Hilton Hotel, Hartford, Connecticut

**May 19-26** — Symposium on Psychiatry and Neurology: A Practical Approach, to be held at Mound Park Hospital Foundation, Inc., 701 Sixth Street, South, St. Petersburg, Florida 33701. For further information address: Neurology, Mound Park Hospital Foundation, Inc., St. Petersburg, Florida 33701.

**May 25** — "Gaylord Day" to be held at Gaylord Hospital and Sanatorium, Wallingford, Connecticut from 2:00 P.M. to 6:00 P.M.

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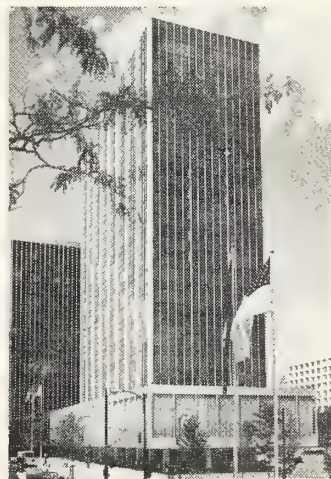
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Saul Feierstein, M.D., announces the opening of an office for the general practice of medicine at 1603 Summer Street, Stamford.

Maurice W. Kearney, M.D., announces the removal of his office for the practice of general surgery to 60 Gillett Street, Hartford.

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## NEW BOOKS IN REVIEW

### **FROM AUSCULTATION TO PHONOCARDIOGRAPHY.**

**Aldo A. Luisada with collaboration of D. M. Mac-Canon, L. M. Rosa, P. M. Shah, R. Zalter. The C. V. Mosby Company, Saint Louis, 1965. 351 pp., 196 illustrations. \$17.75.**

Reviewed by: LOUIS H. NAHUM

This book deals with phonocardiography and how it has produced new knowledge which may lead to revision of classical auscultation. In the phonocardiographic record we have timing with the electrocardiogram and at times with intracardiac pressure pulses. It produces a permanent record which can be compared with previous and subsequent ones and eliminates the differences in auditory acuity of the clinician as well as confusion from changing pathologic and physiologic events which alter sounds. In this sense the phonocardiogram like the electrocardiogram offers additional data to the alert clinician and helps to sharpen his diagnostic acumen. He must become thoroughly conversant with the events in the cardiac cycle so he can relate sounds and murmurs more intelligently to what is going on in the heart at the time we hear sounds and murmurs.

However, after all, the most important data of clinical auscultation were known and correctly evaluated nearly a century ago at the time of Potain. So we have known for a long time the meaning of splitting of heart sounds triple rhythms, opening snap, characteristic rumbling of mitral stenosis, harsh systolic murmurs of aortic and pulmonary valve stenosis, blowing soft diastolic murmurs of aortic and pulmonary insufficiency and soft systolic murmurs of mitral and tricuspid insufficiency. All these have been correctly evaluated before the end of the last century.

The phonocardiogram now gives us sounds some of which we do not hear. But a soft application of an open bell will give up low vibrations, a firm application will give us higher frequencies. To that extent is this not enough to offer the clinician all meaningful sounds he needs to take into account. Should we lose confidence in our auscultation because we do not have access to a phonocardiogram. The author does not say so but in his discussion of the meaning of soft systolic murmurs he hints so. He points out they cannot be "functional," may not be "innocent" even though the heart is normal in size, its electrocardiogram is normal, and the response to exercise is normal.

However, if one applies the Reynold's constant as the author does in explaining the origin of turbulence, it is clear enough that systolic murmurs can arise without a valvular origin. Incidentally the Reynold's constant involves a third factor in the numerator, density of the fluid, which is left out by the author.

On page 55 is discussing the ideal stethoscope he states the ideal bore of the tube as 30-32 mm. but he means 3.0 to 3.2 mm.

In general it is an excellent book on phonocardiography by a distinguished physiologist of 25 years experience. He has

brought the discipline to a high state of development. Perhaps if he persists there may occur some revision of classical auscultation and help us to understand better the data obtained by the stethoscope. It will not replace the stethoscope but make it a more efficient instrument in physical diagnosis of the heart.

As usual a Mosby book is beautifully printed, excellently edited and the illustrations are high class.

**OBSTETRICS. From the Original Text of Joseph B. DeLee, M.D. Author: J. P. Greenhill, M.D., F.A.C.S., F.I.C.S. (Hon.), F.A.C.O.G. Editors, The W. B. Saunders Company, Philadelphia, July 6, 1965, Thirtieth Edition, Illustrations: 1296 on 1193 Figures, 54 in Color, 1246 pp. \$20.00.**

Reviewed by: ORVAN W. HESS

This 1246 page textbook of Obstetrics is the 7th edition compiled by the author. Written in the tradition of Joseph B. DeLee it is essentially a reference book covering most of the important aspects of the specialty. Much new material and many excellent illustrations have been added to make available up-to-the minute information concerning new developments and changing concepts in this field of medicine. The list of contributors includes numerous competent authorities both foreign and domestic. All have the common objective of providing knowledge to guide the physician's management of pregnancy to meet the challenge of achieving a healthy mother and a healthy infant. The book is too voluminous to attempt a detailed review here. In the first section, considerations of anatomy, physiology of the reproductive tract and the physiology and bio-chemistry of the placenta in relation to the fetus are correlated in a manner which serves as a logical basis for rational treatment. A significant chapter is devoted to the complex role of hormones in conception and the interplay of the various components of the endocrine system in the maintenance of pregnancy. Recently developed immunologic and serologic methods for the diagnosis of pregnancy and electronic techniques for monitoring fetal heart activity are described. New research tools have made available more objective data on which to evaluate normal and abnormal labor. Perhaps no chapter is of greater practical importance than that devoted to the detailed description of advances offering greater safety in analgesia and anesthesia. Methods of preparation for childbirth, which complement the armamentarium to make parturition a psychologically non-traumatic experience, are outlined. In the area of complications and pathology of pregnancy further discussion of methods of management of fetal erythroblastosis and other aspects of fetal development seems desirable. Implications of the role of genetics are described.

This textbook indeed represents another monumental effort characteristic of the editor. It should be found very useful to students and practitioners alike.

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# MEDICAL NEWS

## NEW MEDICAL SCHOOLS

Fourteen new medical schools are expected to be in operation in the United States by 1970. These will bring to 101 the nation's total number of schools of medicine. Eight of the 14 schools being planned will provide full four-year programs leading to the M.D. degree. The other six are envisioned as two-year schools of the basic medical sciences. However, three or four of the latter may well progress directly to four-year programs after they have become firmly established.

(1) *The University of Arizona College of Medicine, Tucson*: This is a state-owned, four-year school of medicine currently in development on the campus of the University of Arizona in Tucson.

The first class of students is expected to be admitted in the fall of 1967. The school is being programmed for a class size of 64, although a smaller class will be admitted for the first year or two. Construction of the medical sciences building began in January, 1966, with occupancy expected by the spring of 1967.

The Dean of the College of Medicine is Merlin K. Du Val, Jr., a surgeon, formerly Associate Dean of the University of Oklahoma School of Medicine.

(2) *Brown University, Providence, R. I.*: This is a privately-owned school which offers a program leading to the degree Master of Medical Science. Students completing the program will be qualified to enter the third-year classes of approved medical schools. It is, therefore, comparable to a two-year school of the basic medical sciences.

The six year, integrated program embraces the normal premedical program and the first two years of medical school. The first students were admitted to the first year of the six-year program in the fall of 1963, and will reach the equivalent of the first medical year in the fall of 1967. Thus far, between 15 and 20 students have been admitted to each class. Ultimately a class of 50 students will be admitted annually.

The Chairman of the Division of Biological and Medical Sciences and the Director of Medicine is Mac V. Edds, Jr., Ph.D., who has been for some years a Professor in the Department of Biology at the University.

(3) *University of California, San Diego School of Medicine, La Jolla*: This is a state-owned, four-year medical school being developed on the La Jolla campus of the University of California at San Diego. It will be the fourth medical school in the University of California system, two being in Los Angeles and one in San Francisco.

The school is expected to accept its first class of

32 students in September 1968, and will ultimately enroll 96 entering students annually.

The Dean of the school is Joseph Stokes, III, F.A.C.P., formerly Director of Medical Education at Queen's Hospital in Honolulu, Hawaii.

(4) *University of Connecticut School of Medicine, Farmington*: This is a state-owned, four-year medical school being established as a part of a health center in Farmington, about seven miles west of Hartford. The Health Center will include a four-year school of medicine, a four-year school of dental medicine, and a hospital and outpatient department. The Health Center will be an integral part of the University of Connecticut, the main campus of which is located in Storrs, 25 miles east of Hartford.

The School of Medicine is expected to open in 1968. Initial construction will accommodate 48 entering students in the School of Medicine and 48 entering students in the School of Dental Medicine.

The first appointed Dean was Lyman M. Stowe, who had formerly been Associate Dean of Stanford University School of Medicine. After Dean Stowe's untimely death in June, 1965, John W. Patterson, former Vice Chancellor, Dean and Professor of Physiology at Vanderbilt University School of Medicine, was appointed Dean.

(5) *University of Hawaii Medical School, Honolulu*: This is a state-owned, two-year school of the basic medical sciences being developed on the University of Hawaii campus at Honolulu.

The school plans to admit students to the first medical year in the fall of 1967 or 1968. Although a somewhat smaller class may be accepted initially, there will eventually be 48 entering students annually.

The Dean of the school is Windsor C. Cutting, a pharmacologist, currently Director of the Pacific Biomedical Research Center and formerly Dean of Stanford University School of Medicine.

(6) *The College of Medicine, The Milton S. Hershey Center, The Pennsylvania State University, Hershey*: This is a privately-owned, four-year medical school affiliated with a land grant college, Pennsylvania State University.

Teaching facilities are being planned for an annual entering class of 64 students. The first class of 40 students will probably be admitted in September, 1967.

The Dean of the College of Medicine is George T. Harrell, Jr., F.A.C.P., formerly Dean of the University of Florida College of Medicine.



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(7) *Michigan State University College of Human Medicine, East Lansing*: This is a state-owned, two-year school of the basic medical sciences being established on the campus of Michigan State University in East Lansing.

A firm date has not yet been decided upon, but an initial class will probably be admitted in September, 1967. Ultimately there will be 50 students in each incoming class. The College of Human Medicine will be integrated closely with the general University and particularly with the College of Veterinary Medicine and the College of Natural Science.

The Dean of the College of Human Medicine is Andrew D. Hunt, Jr., formerly Associate Professor of Pediatrics and Director of the Medical Clinics at Stanford University School of Medicine.

(8) *The Mount Sinai School of Medicine, New York*: This is a privately-owned, four-year school of medicine being developed at the Mount Sinai Hospital in New York City. It is the only developing school not affiliated with a college or university.

Admission of the first class of 48 students is set for 1968, with rapid enlargement planned in future years toward a goal of 96 students in each entering class.

The Vice President of the Mount Sinai Center and Dean of the School of Medicine is George James, former Health Commissioner of the City of New York.

(9) *The University of New Mexico School of Medicine, Albuquerque*: This is a state-owned, two-year school of the basic medical sciences being developed on the campus of the University of New Mexico in Albuquerque.

The initial class of 24 students was admitted in September, 1964, and the second class of the same size in September, 1965. Ultimately the school expects to accept 48 entering students each year. The present medical school program has been designed for two years only, but the school expects to move to a full four-year program in the relatively near future.

The Dean is Reginald H. Fitz, F.A.C.P., formerly Associate Dean of the University of Colorado School of Medicine.

(10) *Rutgers—The State University, Rutgers Medical School, New Brunswick, N. J.*: This is a state-owned, two-year medical school, being established on the campus of Rutgers—The State University in New Brunswick.

A pilot class of 16 students will be admitted in September, 1966, the 200th anniversary of the University. A full class of 64 students is planned for the fall of 1967, provided that construction of the main medical school building is completed in time.

Dean of the Medical School is DeWitt Stetten, Jr. Dr. Stetten is a biochemist and was formerly Associate Director in Charge of Research at the National Institute of Arthritis and Metabolic Diseases of the National Institutes of Health.

(11) *University of Texas, South Texas Medical School, San Antonio*: This is a state-owned, four-year medical school in San Antonio, created by an Act of the Texas Legislature in 1959 to take its place alongside the University of Texas Medical Branch in Galveston and the University of Texas Southwestern Medical School located in Dallas.

Present plans are to admit a small entering class of first-year students in September, 1967. Since construction of the medical school will not be complete until 1968, the initial students will probably be housed in temporary or improvised classrooms and laboratories. At full operation there will be 100 students admitted in each entering class.

The Dean of the Medical School is Fitzhugh Carter Pannill, F.A.C.P., formerly Assistant Dean of the University of Texas Southwestern Medical School.

(12) *University of Massachusetts School of Medicine*: Planning complete curriculum for M.D. degree. Maximum enrollment planned for 100; tentative starting date to be announced.

The Dean of the School of Medicine is Lamar Soutter.

(13) *Toledo State College of Medicine*: Maximum enrollment planned for 96. To be announced are the Chief Administrative Officer and the tentative starting date.

(14) *University of California School of Medicine, Davis*: Planning programs to meet requirements for the first two years of the medical curriculum.

To be announced are the tentative starting date and the maximum enrollment planned.

The first Dean of the school will be Charles J. Tupper, F.A.C.P., Ann Arbor, Mich.

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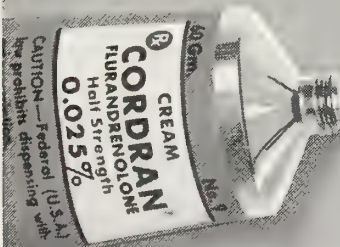
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1965-1966

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# Connecticut Medicine

## editorials

### Saving Lives By Intrauterine Transfusions

Liley<sup>1</sup> in September of 1963 reported the first successful intrauterine transfusion in a case of erythroblastosis fetalis. The method was practical for in utero treatment of an infant severely afflicted with hemolytic disease and seems to have altered profoundly the prognosis for many babies who would otherwise die of their disease before 32 weeks of gestation, a period too early for induction of labor to hold any hope for survival.

Following the withdrawal of amniotic fluid, a radio-opaque substance was instilled into the amniotic cavity. In addition to delineating the fetal outline, the radio-opaque medium was swallowed by the fetus resulting in a demonstration of the small intestine. Using the fetal gastrointestinal

tract as a guide, Liley passed a needle through the maternal abdominal wall, the uterine wall and through the abdominal wall of the fetus. RH negative blood was then instilled into the fetal peritoneal cavity and absorbed into the fetal circulation.

Queenan<sup>2</sup> reports the case of an infant whose life was saved by two intrauterine transfusions. Several other reports of the successful use of this procedure have appeared recently as well as in this issue. Experience in Winnipeg where intrauterine transfusions have been practiced extensively confirmed the value of this procedure, but also demonstrate that there are problems and difficulties involved.<sup>3,4</sup>

Published descriptions of the technique of intrauterine transfusions suggest that it is a relatively simple and safe procedure. In fact however it is not that simple and is not something to be at-

## THE COVER

### PRESENTATION OF THE FIFTY YEAR MEMBERSHIP AWARD

The cover photograph and story for this issue concerns awards for 50 years of membership and service, which were presented to twelve members of the Society during a ceremony at the Annual Dinner of the 174th Annual Meeting and Scientific Assembly, April 26-28 at the Statler-Hilton Hotel, Hartford.

Dr. Orvan W. Hess, New Haven, newly installed president of the Connecticut State Medical Society, is shown in the cover photo, left, presenting 50-year membership awards to, left to right, Dr. Genesis F. Carelli, New Haven, Dr. Daniel P. Griffin, Bridgeport, Dr. Anthony J. Mendillo, New Haven, Dr. Isao Hirata, Sr., New Haven, and Dr. Raymond V. Quinlan, Meriden. Awards were also presented in absentia to Dr. Daniel T. Banks, Bridgeport, Dr. James L. Gilday, Bridgeport, Dr. James R. Miller, West Hartford, Dr. Harry S. Reynolds, Ellington, Dr. Upton S. Reich, Trumbull, Dr. Frank F. Simonton, Enfield, and Dr. Anthony P. Vastola, Waterbury.

There are presently 38 other living physicians who have previously received this award and who reside in Connecticut and other states.

Other veteran members are: Dr. Joseph H. Beaudry, Dr. Abraham Bernstein, Dr. Charles W. Gardner, and Dr. Charles H. Sprague, all of Bridgeport; Dr. Eliot S. Cogswell, Dr. Claude V. Flaherty, Dr. Arthur B. Landry, Dr. Harry L. F. Locke, Dr. Otto G. Wiedman, Dr. Morris Tuch, and Dr. Charles W. Daly, all of Hartford; Dr. John C. Rowley, Dr. H. Gildersleeve Jarvis, Dr. Clinton D. Deming, and Dr. Harold S. Backus, all of West Hartford; Dr. Frederick H. Hynes, Dr. Maxwell Lear, Dr. Albertus K. Boardman, Dr. Marvin M. Scarbrough, and Dr. Ralph W. Nichols, all of New Haven; Dr. George Goldman, Woodmont; Dr. Arthur C. Smith, Danbury; Dr. John F. O'Brien, Waterford; Dr. Maude T. Griswold, Harwinton. Dr. Frank E. Wilson, Wethersfield; Dr. Michael A. Parlato, Derby; Dr. Charles H. Turkington, Litchfield; Dr. Hugh B. Campbell and Dr. Robert R. Agnew, both of Norwich; Dr. Raymond H. Ryder, Waterbury; Dr. Fred M. Smith, Willimantic; Dr. Harold B. Woodward, Bristol; Dr. Jacques H. Green, North Haven; Dr. Herbert Thoms, Stony Creek; Dr. Edward H. Kirschbaum, Santa Barbara, California, formerly of Waterbury; Dr. Thomas Russell, Mt. Dora, Florida, formerly of Hamden; Dr. Wilder Tileston, Carmel Valley, California, formerly of New Haven; and Dr. George A. Leonard, Fort Pierce, Florida, formerly of Waterbury.

tempted by the occasional operator but should be left into the hands of obstetricians experienced in the technique. The fetus of 25-26 weeks is very small and the peritoneal cavity can be an elusive and changing target. It is not unusual according to Bowman<sup>3</sup> to have to make three to four attempts to enter the fetal peritoneal cavity before success is achieved.

After each attempt, X-rays must be taken to demonstrate success or failure. It is obvious that numerous unsuccessful attempts lead to significant X-ray exposure to mother and infant. Clearly, expertness is necessary in order to keep radiation exposure to a minimum and the radiologist can help by careful coning or the use of image intensification.

As there is hazard to the fetus in the procedure, careful selection of patients is essential to include only those babies who seem certain to die before 33-34 weeks of gestation. Previous fetal death from hemolytic disease with a rise of 0.2 or greater in the optical density of the amniotic fluid is an indication of intrauterine transfusion.

All the experience points to the need of examining the amniotic fluid beginning as early as 24 weeks of gestation. Actually where there has been no previous fetal death and in first sensitized pregnancies, case selection can be based only on amniotic fluid examination. After 29 weeks of gestation the prognosis of impending death on the basis of the rise in optical density of the amniotic fluid seems to be quite accurate. Prior to 29 weeks the significance of a given rise in optical density of the amniotic fluid is less certain.

It seems that a given value at 24 weeks of gestation includes more severe disease than the same figure at 29 weeks. If the optical density of the amniotic fluid at 24 weeks is 0.2 or more, Bowman<sup>3</sup> advises a repeat examination in 7-10 days and if the optical density increases in this interval then intrauterine transfusion should be performed. The transfusion of course is designed to supply the fetus with erythrocytes which could not be destroyed by potent antibodies. In Queenan's case at delivery the cord hemoglobin consisted almost entirely of transfused blood.

It is clear that spectrophotometric analysis of amniotic fluid is very helpful in determining the onset of deterioration from erythroblastosis in the fetus and that this has afforded an effective means of selection of fetuses for preterm delivery as well as the prevention of fetal death by intrauterine transfusion.

L.H.N.

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## The Institute Of Biomedical Research (IBR)

On October 11, 1965 the Institute of Biomedical Research (IBR) founded by the American Medical Association was dedicated in Chicago. In the dedication ceremony, four major talks were given by Irvine H. Page, Philip Abelson, Hudson Hoaglund and Rene Dubos. There were two speakers, with remarks, C. D. Leake and W. McDermott.

Dr. Page pointed out that physicians have always known that the quality of their daily practice depends on the results of research, and the wiser among them know that each patient they examine and care for is a problem in research just as truly as the one examined in the most sophisticated and rigidly controlled research laboratory. Each of our patients is a research problem in whom we sort out the mechanisms of disease and try to apply rational therapeutic procedures. For this reason an institute such as IBR will play a major role in producing knowledge of value to every patient and to society as a whole.

He derides the goals such as "beat the Russians," "create a better world image to glorify ourselves," believing them unworthy goals because, the essence of science lies in the fact that if a scientist holds something to be true he must be able to prove it. He emphasizes his belief that diseases of regulation will usher in the next great change in medical thinking, the previous one being that diseases are caused by invasion of the body by a specific organism.

Dr. Abelson after discussing elements in creativity, hails the new Institute because it can provide aspects of an exceedingly favorable environment for investigation which is certain to be fruitful. It will, he believes, make possible important opportunities to achieve superlative creativity through group interaction. He recognizes that there will be freedom from distraction now characteristic of so many universities.

Dr. Leake in his remarks points out that the original purposes of the American Medical Association: to improve the standards of medical training and medical practice will be further fulfilled in the IBR. It recognizes that scientific research is essential to practical every-day medicine and that the more physicians participate in making research possible, the more will the physician participate in it himself and the more effective he will be in the effort we are making for individual and social wel-





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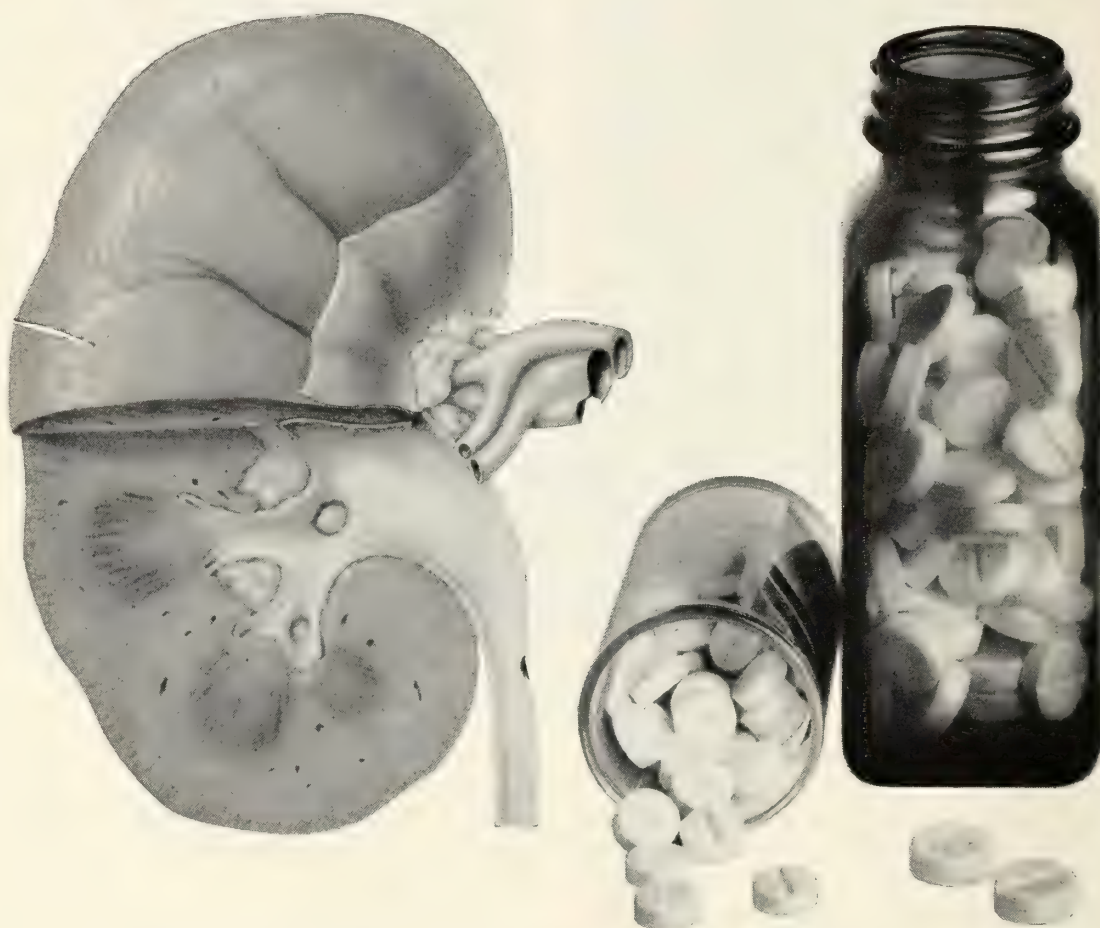
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For example, the Renal Research Program put fifteen years into this search before chlorothiazide became available. But because these years had first led to a greater understanding of basic problems, the desired criteria for chlorothiazide existed before the drug was developed.

Along with other research teams at Merck Sharp & Dohme, the Renal Research Program continues to add new understanding of basic problems—understanding which will lead to important new therapeutic agents.

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fare. His thought is that the IBR will produce important information about ourselves and our environment. As we gain increasing ability to promote good health both physical and mental it will help to make our longer lives more worth the living, both individually and socially.

Dr. Dubos dwelled on the historical trend of the founding of new institutes for research because social or practical needs were not met in universities. He mentioned the Rockefeller Institute, the Agricultural Experimental Stations, the School of Aeronautics at Caltech, institutes devoted to communication theory in the laboratories of Bell Telephone Company or of the International Business Machine Corporation, as but a few of the very numerous illustrations of this trend. Then there is the recent creation of the National Academy of Engineering to supplement the National Academy of Sciences. The latest institute to be founded is a new Biology Center at Washington University, St. Louis, to study how seriously man is contaminating his environment. It is therefore a welcome sign that the American Medical Association has founded IBR to pursue many biological problems the solution of which must enrich our understanding of man, his diseases, his health.

Dr. Dubos goes on to analyze the scope of the IBR as not merely to study the "substance of life," which is theoretical in its philosophy but also the practical aspects of medicine such as surgical and immunological problems posed by tissue and organ transplants. He believes that the success of the IBR will depend upon its ability to deal with unmet social needs especially those that are not met by other institutes. The dilemma faced by medical scientists is that they must always keep in mind both the universal aspects of man's nature and at the same time the problems of health and disease peculiar to each type of society. The most difficult problem he thinks will be how to adapt the internal logic of science to the ill-defined but nevertheless imperative demands of the medical profession and society.

Dr. Dubos having outlined for us what he perceives as the emerging medical problems of our times also indicated his belief that our conventional research attitudes and approaches must undergo substantial modification if our biomedical research is to be helpful in meeting certain of the more important problems. He expressed his deep conviction that to accomplish the difficult task of inventing new approaches, the new departures in research which he envisages will require a considerable increase in the sum of social awareness of the research scientist.

Dr. McDermott's final remarks begin by pointing out the difference between the physicians of today from those of our father's day. Today the

doctor strives to alter the course of a disease whereas formerly his chief task was support to the patient in the form of hope, confidence, comfort and compassion. This isn't quite the whole story because the older physicians had digitalis and some limited but good surgery.

Since 1921 with the discovery of insulin there followed four decades of bursting achievement in the biomedical sciences with increasing ability on the part of the physician to alter and at times overcome the course of disease. But as knowledge has grown, the individual physician can no longer do the whole job alone. Neither is he able to meet the whole medical needs of society. To accomplish this Dr. McDermott believes we must develop new biomedical knowledge, not only that the physician can apply individually to his patient, but knowledge which can permit us to make a true mass attack on such diseases as heart disease, cancer, strokes.

The scientists in the new Institute are not planning to concern themselves in the short run with developing tools for immediate use, for as Flexner pointed out long ago on the "usefulness of useless knowledge," the most esoteric kind of scientific knowledge usually leads to very practical applications. The new Institute will be more than a symbolic affirmation of the debt owed by the medical profession to its biomedical sciences. Neither will it content itself only with broad attempts to unravel the mysteries of nature out of which practical results may follow at some future time. It must find also as McDermott hopes "its own special mission of how to use biomedical science and technology for man's benefit," but frankly isn't this what the medical profession is all about? Why make it appear as though the mission of the physician has left out society. If it had, would we have an IBR founded by the American Medical Association?

L.H.N.

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## Models: A Tool In Biologic Research

Scientific investigation involves posing questions based upon existing data and then searching for answers by experimental means. If there exist no background data, then questions are unanswerable. A question how do we cure cancer is unanswerable because we do not have enough information to ask

a correct question. Arteries are both viscous and elastic. What the function of viscosity is has not yet been elucidated. However, knowing they are viscous permits us to ask whether viscosity is involved in energy dissipation during each cycle and whether the viscous property influences the aortic pressure curve.

Rods and cones in the retina have different shapes. We do not yet know anything about the relationship among size, shape and function of cells. But we could ask whether visual acuity is influenced by the size and spacing of retinal cells. We do not know what happens to the potential generated in each heart cell in relation to the total field function, but we do know the potential from the surface is predominant and we can ask which cardiac areas are specially represented in the various leads. In each instance the tool used to determine the legitimacy of the questions was a model: a retina, an aorta, a heart shell placed in its appropriate location inside the chest.

How does a model help to ferret out the legitimate problems and thus help the investigator direct his attention to their solution? Two dimensional models are found in every test-book, flow diagrams, models for organ systems for glucose metabolism, enzyme systems. Mathematical equations have been used as models for nerve action, population interaction, bacteria-host interrelationship. Three dimensional reproductions have clarified relationships in the brain, in embryos, in the eye, in the aorta, in the electrocardiographic field function. So long as the tool represents in simplified form a portion of a real system, while remaining faithful to a pattern of measurement on the system, the tool is a model and it can serve to facilitate research on a real system.<sup>1</sup>

If one wishes to study the angles at which arteries branch in a parent system an arterial cast will suffice. If one wishes to observe regions of turbulence, a more complex model is necessary, so that the cast not only retains the angles, but must be transparent and must permit flow of labelled fluid or may have to be studied with extensive mathematical equations. Suppose the highest turbulence is found at high angled branching areas. The question immediately follows as to whether this is also true in the real arterial tree with its variations of flow in systole and diastole.

Even though the complex model of the arterial system is much simpler than the real system, studying it will usually include relationships either obscure or unsuspected in the real system.<sup>2</sup> For example the transparent cast with flowing fluid reveals not only the location of turbulence but also the number of permissible branches. The investiga-

tion has more time for a thorough examination of the model than of the actual system which deteriorates too fast in vitro to permit similar leisurely thoroughness. The longer exposure increases the chances for discovering unsuspected relationships. Besides, the model can be made transparent making turbulence easy to see but difficult to measure in the real system.

The study of tissue conductivity in electrocardiography became too complicated by measuring a variety of individual tissues. A model dipole introduced into the body at once revealed that the fixed function on the body surface was that of dipole. This clarified the homogeneity of tissue conductivity but also that the heart itself was a much more complex source of current.

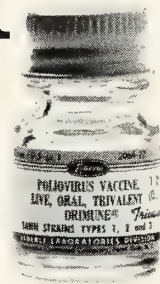
When an investigator recognizes this tool, the model can call attention to hidden properties of the actual system. He is stimulated to study the model in great detail. As he does this the value of the model will increase, for the revelation of hidden properties of a real system through the use of models comes only after thorough investigation of the model's behavior. Then suddenly important questions arise that were not thought of before. A close study of the arterial cast reveals greater turbulence at branching points. Do real arteries have as much turbulence? Do the viscoelastic properties of real arteries decrease or increase the turbulence? Is the transparencies of the cast responsible for the turbulence? Is the turbulence responsible for the increased incidence of atherosclerosis at branching points? The model acts in a certain way. Does the real system act in the same way? If it does not, why not?

In short, the model helps to call attention to elusive details and permits the formulation of working hypotheses. But it differs from verbal hypotheses by never attempting to match reality perfectly. In this way it often requires and invites mathematical assistance. The mathematics may be very simple such as measuring the dimensions of the cast and these provide the means for predicting numerical values of the hidden properties sought for in the real system. Such values are necessary to test the validity of the model. If discrepancies appear between the model and the real system an alternate model is called for. Similarly when experiments suggested by the model when carried out in the real system show discrepancies and the model is too simple, an alternate model is called for.

The rigid arterial cast will not help analyze aortic pressure curves because arteries have viscoelastic properties and blood flow is pulsatile. Thus the model with constant flow in rigid tubes must be replaced by a mathematical analysis with the



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more realistic conditions. If the model of a single dipole does not correspond with the complex source of current generated by the heart, then the model needs to be changed to two or more dipoles placed in various parts of the area occupied by the heart.

Sometimes it is impossible to devise a model consistent with all current data. Then what does the model maker do? He takes the set of data easiest to reproduce and builds a model consistent with this particular set and other models for other sets of data requiring repetition of experiments is indicated. It should be pointed out that two or more models are built only to facilitate research not to substitute for reality.

When more than one model is needed to investigate the reality it signifies that we are at a stage of insufficient knowledge and we are not yet able to fit all data into a single system. But the indicated experiments will ensure progress towards a universal, more efficiently than without a model at all. Every now and then a multiplicity of models leads to a single model, but not until a "breakthrough" is discovered by some brilliant mind. The "simple" model has been termed a paradigm. Einstein's theory of relativity, Schroedinger's wave mechanics, Watson and Crick's helical model of the DNA molecule are of this type.

When an investigator has developed a model consistent with all currently known data, he will have an instrument for close leisurely study of the system of interest to him. He can measure all the measurables in the model using whatever mathematics he can from his own knowledge and that of his mathematical collaborators.<sup>3</sup> He will compute the behavior of the model under a variety of conditions preferably that expected in vivo. The measurements he obtains in the real system will either match or deviate from his predictions. But whatever the result the model has helped to frame the type of questions to ask of his real system and to find the path for arriving at the answers. This of course involves numerous revisions after repeated exposures to the real system, one model giving way to another, each getting closer to the real system.

The model then performs the function of eliminating inconsistencies in experimental design, of evaluating alternate hypotheses and of following reasonable inferences to avoid conclusions which otherwise might be vulnerable.

L.H.N.

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## The Septophrenic Fibrinolyticist

A number of physiologic systems work in harmony to maintain blood fluidity and at the same time the potential to form clots. These include after injury, tissue "hormones", platelet factors and "hormones", the blood coagulation system, the fibrin stabilizing systems and the fibrinolysin system.<sup>1</sup> Since little information of all this has found its way into medical text-books, it is worthwhile to see how the clinician must approach the problem of fibrinolysis when he is confronted with a patient who has suffered a venous or arterial occlusion for he must make a decision what to do, here and now. Moser<sup>2</sup> calls such a clinician a septophrenic fibrinolyticist. By septophrenic he means a condition in which seven separate scientific "personalities" vie for the possession of the scientific psyche, with the danger that anyone personality may do so to the exclusion of the other six: The physiologist, the biochemist, the pharmacologist, the pathologist, the immunologist, the nutritionist, and the clinician. Obviously, the clinician who has a patient that is ill must be aware of the other six personalities, but must also be guided by the need to solve an individual's problem.

The physiologist is concerned with the normal functions of the fibrinolytic system and the factors which regulate its activity. Thus far the major function attributed to fibrinolysis is the prompt removal of fibrin from the vascular system, from various ductal structures, urinary, mammary, salivary, bronchial, etc. He postulates that fibrin formation is balanced by fibrin dissolution via the fibrinolytic system and alterations in this system may promote either a thrombotic or a hemorrhagic diathesis. There is abnormal fluctuation in fibrinolytic activity in young subjects, in patients with diabetes and Laennec's cirrhosis but the full meaning of this circadian rhythm has yet to be clarified. Why exercise increases fibrinolytic activity is still unclear and why occlusion of a limb by a cuff raises fibrinolytic activity is not yet answered although Moser believes it is due to accompanying acidity.

The biochemist is beset with problems of improved assays for tissue activators of plasminogens and the difficulty is knowing that what he sees in vitro is a model of what occurs in vivo. The plasma of a patient who has received a fibrinolytic agent such as urokinase may contain a complex mixture of activator activity, plasminogen, plasmin bound and "free" antiplasmin, and even activator inhibitors.

The pharmacologist is searching for agents that are effective in promoting dissolution of unwanted fibrinous deposits and drugs which can block excessive fibrinolytic activity. Then he needs to establish toxic-therapeutic ratios of such compounds. There are agents other than enzymes which may enhance in-vivo fibrinolytic activity sufficient to promote thrombolysis. Pyrogens, epinephrine, other sympathetic amines, nicotinic acid, all seem to release activators of plasminogen from tissues but as yet none qualifies as an acceptable therapeutic agent in man. Phenyl-butazone has recently been suggested as a non-enzymatic fibrinolytic agent but does not produce such an effect in every patient. The field is fraught with difficulty because of individual differences as well as duration of dose vs. total dose, the former being more important. Finally is the question of drug synergism. For example, heparin potentiates thrombolytic capabilities of streptokinase, plasminogen mixture in dogs.

The pathologist "psyche" must be an integral part of the clinician's outlook. The clinician must recognize that a fresh "red" thrombus in a vein which is primarily a fibrin network with entrapped cellular elements is likely to be more susceptible to fibrinolytic attack than a white thrombus in an artery which is formed primarily by platelet aggregates. The pathologist knows that once a clot is endothelialized it is not susceptible to thrombolysis. Neither is an organized clot. He also is aware that arterial occlusions are caused also by subintimal hemorrhage, by embolism of atheromatous material or pieces of old organized thrombi that have been dislodged perhaps causing spasm as well. Obviously the most successful thrombolytic regimen cannot relieve an arterial obstruction due to a non-thrombotic pathologic process.

The immunologist at present has little to offer the clinician except perhaps to discover the sources and distribution of urokinase, plasmin and plasminogen in man. He may clarify the role of fibrin in such immunologic disturbances as rheumatoid arthritis and collagen vascular disorders in which tissue injury and repair are going on all the time.

The nutritionist has much to offer the clinician especially in the area of the relationship between dietary lipids and atherosclerosis and linolenic acid and platelet adhesiveness. There are many observations that indicate that certain lipids may not only promote coagulation, but also may inhibit fibrinolytic activity. Moser found that milk-cream ingestion truly reduces fibrinolytic properties of blood in young subjects and that increased lipid content of blood decreases the susceptibility of thrombus to fibrinolysis. These growing number of links between lipid metabolism, coagulation,

fibrinolysis, and atherosclerosis are stimulating and must be kept in attention by the clinician.

The clinician of course has to deal with the patient bearing all these previous "psyches" in his own mind. It is his responsibility to make a diagnosis of an intravascular clot, which as noted above is at present extremely difficult especially on the arterial side. In this area diagnostic progress has been extremely limited. Another of the clinician's dilemmas is how to distinguish between therapeutic response and natural cause of the disease. This is especially true with respect to thrombo-embolic venous disease in which heparin and coumarins seem to work fully as well as any present thrombolytic enzyme.

The second responsibility of the physician is when to decide to use enzymatic fibrinolytic agents. On the other hand it is painful to remain inactive and be reduced to the uncertainty of Hamlet. The clinician is not in the enviable position of the basic scientists who can experiment, contemplate, and imagine. He must try to help at the same time avoiding doing harm.

As we view Moser's<sup>3</sup> recommendations about the current view of available enzymatic thrombolytic agents, we find ourselves not totally convinced. For example, he employs them in certain forms of acute deep venous thrombosis, pulmonary embolism and peripheral arterial occlusions. However, he is strictly an experimental clinician and has not yet had the opportunity of comparing his results with more conservative methods. His aim at present is to use his clinical ingenuity to overcome problems encountered at the basic level. He is seeking for the proper dosage regimen of a thrombolytic agent which will at one and the same time achieve thrombolysis without inducing a hemorrhage diathesis. For this he needs close, complex biochemical monitoring of coagulation fibrinolytic parameters.

Moser is especially interested in closed circuit perfusion of involved limbs where a high concentration can be attained with no systemic coagulation disturbances. Perhaps with technologic advance adaptation of this technique to other vascular areas may be possible. Then perhaps local instillation of agents directly at sites of thrombotic occlusion may permit high local activity while limiting the risk of hemorrhage elsewhere.

It is obvious from this that the bedside clinician has not yet been favored by agents which are ready to be employed in fibrinolytic therapy. Heparin and phenylbutazone and in the future other non-enzymatic fibrinolytic agents must still remain his mainstay in treating thrombosis.<sup>4</sup> Perhaps the development of improved methods for diagnosing thrombo-embolic disease and delineating its natural





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### Warning

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Pyrazole compounds may potentiate the pharmacologic action of sulfonyleurea and sulfonamide-type agents and insulin. Patients receiving such concomitant therapy should be carefully observed for this effect.

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The most common adverse reactions are nausea, edema and drug rash. The drug may reactivate a latent peptic ulcer. Infrequently, agranulocytosis, generalized allergic reaction, stomatitis, salivary gland enlargement, vertigo and languor may

occur. Leukemia and leukemoid reactions have been reported but cannot definitely be attributed to the drug. Thrombocytopenic purpura and aplastic anemia are also possible side effects. Confusional states, agitation, headache, blurred vision, optic neuritis and transient hearing loss have been reported, as have hepatitis, jaundice, and several cases of anuria and hematuria. With long-term use, reversible thyroid hyperplasia may occur infrequently.

### Average Dosage in Rheumatoid Arthritis

**Initial:** 3 to 6 capsules daily in divided doses. It is usually unnecessary to exceed 4 capsules daily. A trial period of 1 week is adequate to determine response; in the absence of favorable response, discontinue.

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possibly be increased by meprobamate. Grand mal seizures may be precipitated in persons suffering from both grand and petit mal. Prescribe cautiously and in small quantities to patients with suicidal tendencies.

**Side effects:** Drowsiness may occur and, rarely, ataxia, usually controlled by decreasing the dose. Allergic or idiosyncratic reactions are rare, generally developing after one to four doses. Mild reactions are characterized by an urticarial or erythematous, maculopapular rash. Acute nonthrombocytopenic purpura with peripheral edema and fever, transient leukopenia, and a single case of fatal bullous dermatitis after administration of meprobamate and prednisolone have been reported. More severe and very

rare cases of hypersensitivity may produce fever, chills, fainting spells, angioneurotic edema, bronchial spasms, hypotensive crises (1 fatal case), anuria, anaphylaxis, stomatitis and proctitis. Treatment should be symptomatic in such cases, and the drug should not be reinstituted. Isolated cases of agranulocytosis, thrombocytopenic purpura, and a single fatal instance of aplastic anemia have been reported, but only when other drugs known to elicit these conditions were given concomitantly. Fast EEG activity has been reported, usually after excessive meprobamate dosage. Suicidal attempts may produce lethargy, stupor, ataxia, coma, shock, vasomotor and respiratory collapse.

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course will come. Perhaps modern technologic ingenuity to render thrombolysis safer and more effective will also come. Then the clinician will become the "compleat fibrinolyticist."

L.H.N.

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The Spleen As A Production Site Of An Erythropoietic Factor

It has been known for a generation<sup>1</sup> that the spleen influences red cell production by a stimulating action on the bone marrow. The possibility has been raised that the substance generated by the spleen does not directly affect bone marrow but must first be processed in the liver before it can induce red cell production. In order to test this hypothesis it is necessary to have an index of red cell production, to obtain an acellular extract of spleen and to inject it into mice with and without the liver. De Franciscis, et al. prepared an acellular extract from the spleen of a fresh killed animal, homogenized it in a blender, centrifuged it and added sucrose to obtain a 0.25 m. concentration. To determine red cell production he studied the reticulocyte response pattern and alterations in the hematocrit.

Previously the author subjected mice to x-irradiation of the total body and showed that homogenates of only spleen and liver among several organs tested from several different species are protective in action against X-ray mortality. They also found that an acellular preparation from the spleen was active when tested in animals of another species. Could this protective action be due to a substance in the spleen which stimulates the bone marrow to produce red cells and if so how does it do this?

De Franciscis proceeded to compare effects of acellular homogenates of several tissues on red cell production. They prepared acellular extracts of liver, kidney and muscle from rats, mice and calves, which they then injected into the peritoneal cavity of mice as a control. They counted the reticulocytes, established hematocrit values and red cell numbers were obtained daily for four days. In one group of mice that were splenectomized fifteen days before, they injected sucrose homogenates from rats and mice. In another group a further purified homogenate of calf spleen was tested.

The results were clear and unequivocal. Saline, muscle and kidney extracts did not increase reticulocyte counts, hematocrit or red cell numbers. Neither did the liver itself if injected in splenectomized mice.

It was clear enough that without the spleen the liver extracts produced no erythropoietic stimulation. On the other hand, there was a pronounced and significant increase in reticulocyte response in mice when they were treated with spleen extract and with liver extract of normal rats. This increase was as great as that observed by Winkert, et al, after they treated rats with fourteen erythropoietic units of human urinary erythropoietic stimulating factor per day. Extracts from other organs such as muscle, kidney, produced no erythropoietic effects.

It is clear that the liver by itself is unable to stimulate red cell production in the absence of the spleen. The spleen alone also cannot stimulate erythropoiesis. However when both spleen and liver are intact then erythropoiesis goes on. The substance which the spleen elaborates and is then processed by the liver to stimulate red cell production is thought by De Franciscis to be hypoxilienine. If this is the substance it is different from erythropoietin.

There are other mechanisms known to stimulate erythropoiesis some of which are unknown. For example, low oxygen tension whose effects are seen at high altitudes and in children and adults with abnormal lungs, leads to polycythemia but the mechanism is unknown. However the plasma from animals rendered anemic by various means will stimulate red cell production in recipient animals.<sup>2</sup> This effect has been ascribed to the presence in such plasma of an agent called erythropoietin previously thought to arise in the kidney and purified preparations have been obtained of this substance from sheep and rabbit plasma and from urine. The purified preparation from sheep plasma had the properties of a mucoprotein.

This new erythropoietic function of the spleen has certain medico-legal as well as physiological aspects because of the cases of traumatic spleen rupture which necessitates splenectomy. There surely exist other sources of erythropoietin besides the spleen, since splenectomized patients seem not to develop anemia readily. What element in erythropoietic reserve that can be attributed to the spleen still remains to be elucidated.

L.H.N.

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## Pulmonary Surfactant And Hyaline Membrane Disease

Many physiologists and clinicians think of the pulmonary circulation as a set of pipes delivering blood to the alveolar capillaries, collecting it and sending it on to the left atrium and left ventricle and having nothing to do with nourishing tissues through which it passes. However, there appeared some remarkable observations that brought this view into question. One is that when occlusion of one pulmonary artery was produced, it led to a decrease of ventilation in that lung—not surprising—but what was a surprise to everyone was that the lung at first was atelectatic and at the same time markedly congested. The lung however did not die and gradually over some months the ventilation of the lung increased, its appearance improved and it became reasonably normal although somewhat scarred.

The explanation for this phenomenon, confirmed by anatomists, was that the bronchial arteries supply the airways down to and including the terminal bronchioles, and that the pulmonary artery supplies the alveoli, alveolar ducts and the respiratory bronchioles. This view is easy to confirm since drugs that constrict smooth muscle when injected into the pulmonary artery affect only alveolar ducts, but when injected into the bronchial arteries, instead affect the airways only down to and including the bronchioles.

To function properly the alveoli and alveolar ducts require less than one-seventh of total pulmonary blood flow, a figure so low as to make it doubtful that pulmonary ischemia and collapse could ever occur in adult life.<sup>1</sup> However, regional blood flow can be too little to sustain cell function. The alveolar cells of the lungs, especially, have a high metabolic rate and do not tolerate ischemia well, are active in the syntheses of phospholipids and of dipalmitoyllecithin.<sup>2</sup> In some way not yet understood this substance reaches the alveoli and lines them with a monomolecular layer. In this form it has the unique property of decreasing surface tension and preventing collapse of alveoli during expiration.<sup>3</sup>

It is appropriate to inquire why the surface active material which lowers surface tension prevent the collapse of alveoli? Elastic fibers of the lungs cause recoil but this does not account for the unusual phenomenon that air filled lungs do not collapse. They will collapse however if saline fills the lungs. The reason for this is that saline filled lungs exercises surface tension which causes collapse. The air filled lungs show a surface tension which goes down to zero and no collapse occurs. The surfactant produced by alveolar cells is therefore an anti-atelectasis factor.

When alveolar cells receive less than the minimal amount of blood necessary for their nutrition then Comroe points out one of two things can happen: The quality or quantity of surfactant formed is not proper or else pulmonary capillaries become leaky, plasma enters the air space and plasma fibrinogen interacts with the pulmonary surfactant to cause both an inactivation of the surfactant and an inhibition of fibrinolysis.<sup>4</sup> The result is that alveoli collapse become filled with fibrin threads, the so-called hyaline membrane.

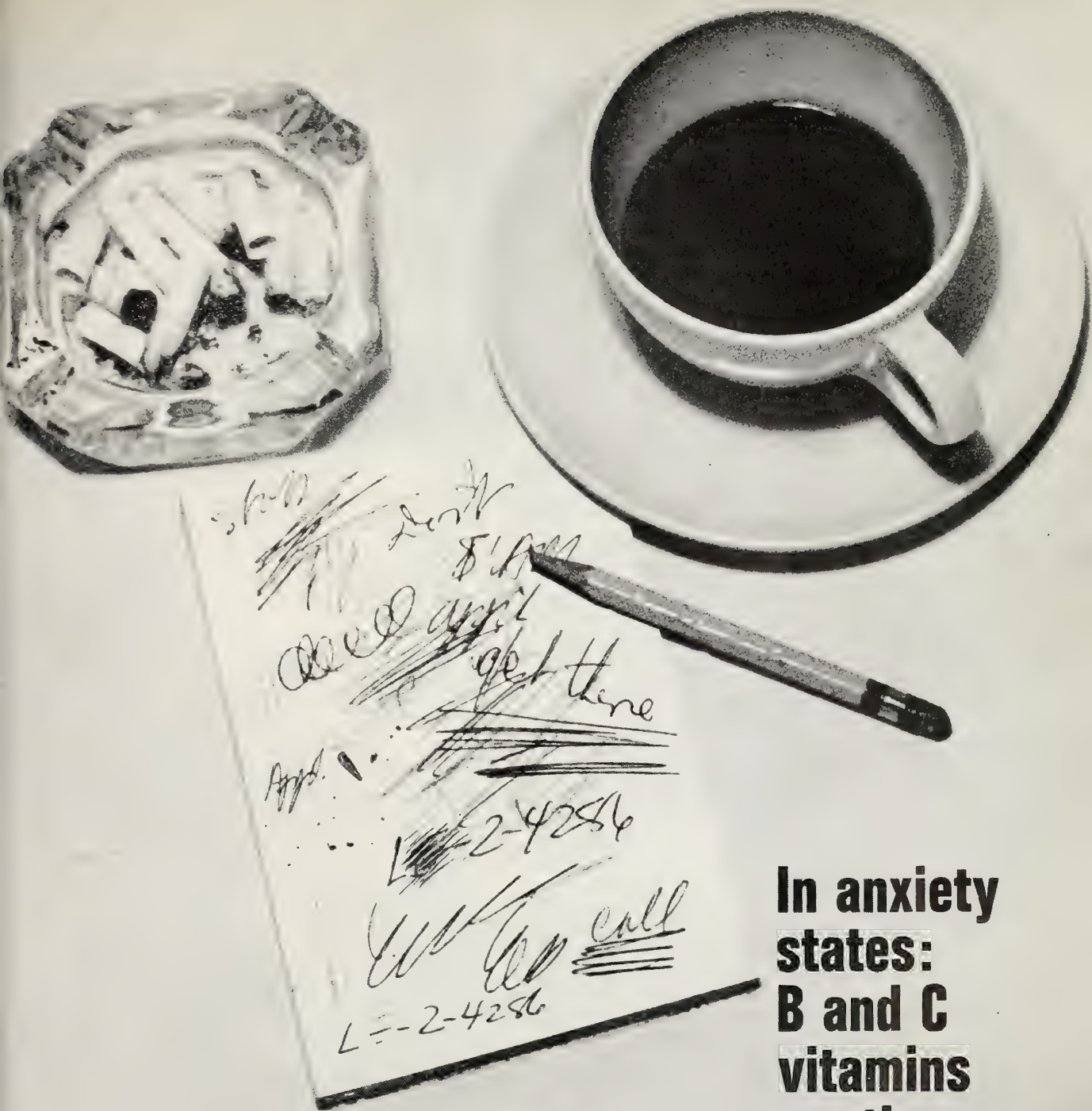
In the newborn, pulmonary blood flow can be less than the minimal required for nutrition because there is a large by-pass—the ductus arteriosus—which can shunt all the right ventricular output when it cannot go through the pulmonary circulation. In such an event ischemia of the newborn lung could become a cause for atelectasis or as it is termed respiratory disease syndrome.

In 1964 Clements, Tooley and Klaus<sup>5</sup> became convinced that the pulmonary surfactant was in fact dipalmitoyllecithin or a chemical very similar to it. They reasoned that if inactivation of this phospholipid was a major factor in newborn lung atelectasis which gave rise to respiratory disease syndrome, one ought to be able to improve this condition by propelling additional dipalmitoyllecithin into the lungs of the newborn infants suffering from respiratory distress. This replacement type of therapy helped some infants but not all. The failures were probably due to inability to get enough of this material into the alveoli which were already collapsed as well as the presence of material in the alveoli, perhaps plasma fibrinogen, which inactivated some or all of the surfactant that did reach the alveolar surfaces.

They encountered another serious difficulty, great resistance of the pulmonary circulation to the flow of fluids through it. This they found in lungs of babies who died of the respiratory distress syndrome, as well as in living babies whose pulmonary blood flow was reduced to only one-third of that in healthy babies. Once pulmonary vaso-dilators were infused intravenously previously retained CO<sub>2</sub> began to pour out, and PO<sub>2</sub> rose leading to a marked decrease in wasted ventilation.

However in some babies sustained and adequate pulmonary ventilation was obtained only by intravenous administration of sodium bicarbonate.<sup>6</sup> This confirmed an idea that acidosis is a potent pulmonary vasoconstrictor. Clements, et al. thus arrived at a method of combating respiratory distress syndrome by combating pulmonary ischemia, atelectasis and acidosis. The hyaline membrane which occurs in babies with the respiratory distress syndrome can also be produced experimentally in dogs following pulmonary artery occlusion which





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\*\* Denotes resolution of at least 50%.

\* Denotes resolution up to 50%.

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| Number of Cases             | 14     | 24    | 18     | 14     | 9      | 3      | 7      | 4      |
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The types of psoriasis included (parentheses indicate number of cases); Generalized (31), Palms and soles (7), Legs and feet (18), Scalp and ears (27), Groin (3), Neck (5) and Vulva (2).

Keranil Ointment appears to be most effective against the typical psoriatic plaque characterized by heavy scales. Furthermore, it appears to benefit both palmar and plantar plaques as well as intertriginous lesions and to be least effective against the small guttate lesions.

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**Availability:** Keranil ointment is available in one ounce jars as a 10% concentration of choranil in a polyoxyethylene carrier.

#### References:

Teichmann, W. O. and Horvath, P. N.: Southern Medical Journal 50, 1521 (1957).

*Literature and samples on request.*

# Salem Pharmacal

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also causes pulmonary ischemia, atelectasis and acidosis.

At the present time we do not yet know whether pulmonary ischemia in babies comes first and is causative or whether it comes later as a result of hypoventilation, hypoxia, and acidosis. If it comes first as it does in the dog experiments, it is a sequel of asphyxia of the fetus or fetal hypotension, or is it due to a failure of fetal pulmonary vessels to relax normally at birth.

We are still unclear about the mechanisms which, at the birth of a baby, simultaneously cause pulmonary arterioles to dilate and ductus arteriosus and the umbilical arteries to constrict. The reason why we are unclear is that reflexes may be involved as well as the high oxygen concentrations which are known to dilate pulmonary arterioles in the fetus and to constrict the ductus arteriosus and umbilical arteries.

We thus see that in deficiencies of surfactant there is evidence of inadequate alveolar perfusion, leakage into alveoli of plasma components or both. Alveolar capillary perfusion in turn depends upon pulmonary vascular resistance which increases markedly with inadequate oxygenation and high acidity of the arterial blood. Combatting inadequate perfusion by reducing vascular resistance, overcoming acidity of the arterial blood by sodium bicarbonate and instilling surfactant into the pulmonary tree, is the triad upon which depends successful treatment of the respiratory distress syndrome in the newborn. Out of basic science study of a newly recognized constituent of lung, has come a practical way of saving lives of some newborns.

L.H.N.

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## The Effect Of Emphysema Upon Venous Return

The forces which operate to return the blood to the heart have interested physicians for a long time, including the role of respiration. The physician is a close observer of the neck veins and watches

them collapse during inspiration in the normal recumbent subject, but they do distend in certain patients with a variety of disease states in particular in diseases of the pericardium. What happens in the inferior vena cava has been inferred until now so that in a given patient, at what point intra-thoracic pressure will be sufficient to collapse and obstruct inflow is only conjectured.

In a recent communication Nakhjavan, et al.<sup>1</sup> investigated by cineangiography of the inferior vena cava (IVC) the influence of respiration on venous return in normal man and in patients with emphysema. In most cases flow from the abdomen to thoracic IVC was continuous and obviously greater during inspiration. However, in some patients characterized by gross hyperinflation of the lungs, the pattern of flow at the level of diaphragm was completely reversed being much reduced or completely arrested during inspiration. The question of course arose as to the significance of this phenomenon and what can be its mechanism.

There were fifteen patients with pulmonary emphysema that were compared with ten normal subjects. The ten normal subjects and nine of the patients with pulmonary emphysema showed a continuous flow from abdomen to thorax in the IVC throughout the respiratory cycle and invariably greater flow during inspiration. After the IVC was narrowed at the diaphragm and 4-5 cm distally. Two patients in right heart failure also showed continuous flow throughout respiration with an inspiratory increase, but the IVC was more dilated as is to be expected in venous congestion. The clearance of the radioopaque material was retarded and the hepatic veins remained filled for several breaths following the injection.

In six emphysematous patients, however, the period of maximum flow was not during inspiration but rather during expiration. In the control subjects inspiration was seen to cause relative emptying of IVC and its refilling during expiration. As the IVC partially emptied, the right atrium became better filled. In the six emphysematous patients, the transmural IVC pressure increased during inspiration as the transmural right atrial pressure decreased. What could be the mechanism of this abnormal flow? Nakhjavan, et al. came to the conclusion that there was severe hyperinflation of the lungs which in turn caused a depression of the diaphragm, and interference with upward flow in IVC.

What can be the hemodynamic significance of this interesting phenomenon. We know that in patients with pulmonary emphysema any light exertion can initiate great respiratory efforts and intra-thoracic pressure may become markedly elevated

during expiration. If upward flow can occur only in expiration when intra-thoracic pressure is high and not during inspiration, then during exercise the mean IVC pressure may become considerably elevated and may reach values higher than were recorded in these patients at rest. Indeed it is possible that this may be the mechanism of production of the peripheral edema in patients with emphysema who have no pulmonary hypertension or heart failure.

If it is true that in some patients with emphysema flow is greatest into the chest during expiration, then the normal splitting of the pulmonic second sound should be abolished in these patients. Normally inspiration is accompanied by an increase in the interval between the two components of the second sound presumably because of better right ventricular filling and increased stroke volume. However, in patients where flow in IVC and filling of the right ventricle is reduced during inspiration one would expect the normal inspiratory increase in the second sound interval to be abolished. This is exactly what happened in the two cases of emphysema in which they could record the pulmonic second sound.

L.H.N.

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## The Role Of The Sympathetics In Premature Systoles

There are certain types of premature systoles which are invariably associated with an underlying cardiac disorder. These are multifocal or paired especially if the premature systole falls in the vulnerable period. This type is readily apparent in the electrocardiogram. On the other hand it has been noted that various extracardiac factors also increase the incidence of premature systoles, such as anxiety states, dissipation, and certain common drugs. Because of the frequency and benignity of these arrhythmias their actual incidence is virtually undocumented. Most physicians agree that there is rarely a healthy individual who has never exhibited premature systoles. These come and go without detectable reason and are of no prognostic significance.

In normal hearts sudden death due to emotional strain is extremely rare, although Katz<sup>1</sup> observed paroxysmal ventricular fibrillation in an individual whenever an electrocardiograph machine was wheeled into the room. The recognition by the patient with cardiovascular disease that sudden

death may occur has a profound effect on his mental state. Furthermore, disorders of rhythm resulting from emotional disturbances or myocardial dysfunction may in turn result in mental symptoms which can further aggravate this condition.

For centuries it has been recognized that the heart is potentially susceptible to emotional stimuli and one of the earliest observations of emotion induced tachycardia was made by Avicenna in the 10th Century.<sup>2</sup> Ever since then careful observation of patients with palpitation may reveal a high incidence of cardiac arrhythmia at the time of palpitation. Anxiety may precipitate ectopic rhythms in normal hearts as well as those with structural disease. Apparently similar factors are operative in both groups of patients, although patients with cardiac abnormalities are more vulnerable to this development. The factors involved in the genesis of these arrhythmias become clear if one considers the experimental mechanisms involved in their production.

Nahum and Hoff<sup>3</sup> showed that the ventricular tachycardias and ventricular fibrillation caused by inhaling benzol will not occur if the cardiac sympathetics are cut and the adrenals removed. They studied arrhythmias caused by other agents and in each instance found that without adrenergic activity no cardiac arrhythmias could be produced. We know that ventricular arrhythmias due to digitalis is aggravated by sympathomimetic drugs and that surgical ablation of the cardiac sympathetics or depletion of the myocardium of its nor-epinephrine content by reserpine<sup>4</sup> can reduce or abolish cardiac arrhythmias. We have then an operative hypothesis to work with: that cardiac premature systoles or tachycardia are the result of the interaction of two factors, the sympathetic nervous system and an exciting agent.

If epinephrine and nor-epinephrine—the sympathetic neurohormones and another substance together are responsible for premature systoles and tachycardias, then in all situations when premature systoles occur we must seek out the factors responsible for heightened sympathetic tone as well as other agents acting synergistically with the sympathetic neurohormones to generate ectopic impulse formation. Premature systoles have been known to occur as a part of a reaction to pain, elation, fear, resentment, humiliation, excessive hostility, compulsiveness, anger, depression, excessive fatigue, all situations with which both the sympathetics and an irritant agent may exist. Any situation in a patient's life in which a sudden acute exacerbation of tension may be expected to result in the production of arrhythmias.

Premature systoles may be an early sign of myocardial disease especially if they fall during the





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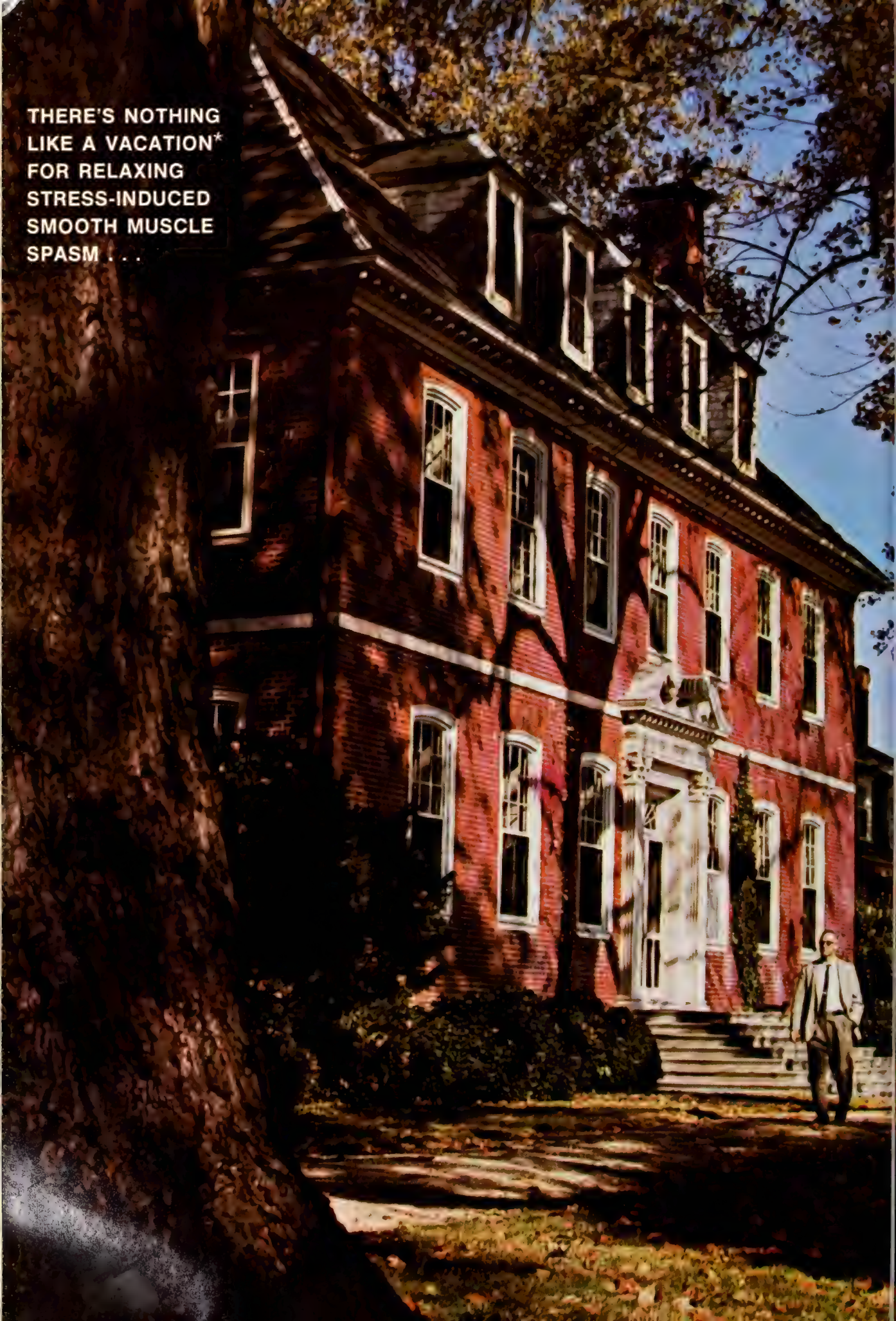
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(warning: may be habit forming)

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atropine sulfate . . . . . 0.0582 mg.  
hyoscine hydrobromide . . . 0.0195 mg.  
phenobarbital . . . . . (3/4 gr.) 48.6 mg.  
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**BRIEF SUMMARY:** Blurring of vision, dry mouth, difficult urination, and flushing or dryness of the skin may occur on higher dosage levels, rarely on usual dosage. Administer with caution to patients with incipient glaucoma, or urinary bladder neck obstruction. Contraindicated in acute glaucoma, advanced renal or hepatic disease, or a hypersensitivity to any of the ingredients.

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\*This one at Westover, elegant Colonial Virginia plantation, located on the James River near Richmond. Built in the early 1730's by William Byrd II, founder of Richmond, it is now the home of Mrs. Bruce Crane Fisher.

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vulnerable period in the electrocardiogram. Obviously a complete examination is indicated. The physician then possesses the necessary information and prestige to explain these disturbances of rhythm to the patient and every effort should be made to assure the patient that he may lead a normal life with safety. It may even be worthwhile for the physician during the examination not to listen too long to a particular region of the chest or relate significant findings to the patient.

All activity on the part of the physician should be directed to allaying fear in the mind of the patient, thereby reducing the sympathetic tone. It may require also manipulation of the life situation and efforts to help the patient deal more constructively with his problems and conflicts. Nothing will convince the patient so readily of the innocence of his arrhythmia as the lack of restrictions on his life. There are some instances when premature systoles may engender an unpleasant impact of blow on the chest to produce a throb from the oncoming beat and make the patient very uncomfortable. Then his awareness of the disturbance may be reduced by phenobarbital or other appropriate tranquilizers. It is rare however that an anti-arrhythmic agent for the treatment of premature ectopic beats due to anxiety becomes necessary.

Having reduced as much as possible the factor of heightened sympathetic tone sometimes pharmacologically if needed,<sup>3</sup> the next step requires the elimination of agents that are synergistic with the catecholamines. One of them is nicotine<sup>5</sup> in which there is a known discharge of epinephrine after heavy cigarette smoking. Of course if there is already heart disease present the heart is more vulnerable to ectopic beating due to nicotine. In such instances especially if there is atrial premature systoles or tachycardia, digitalis may be needed in addition to cessation of smoking.

Caffeine is known to stimulate the myocardium directly. It causes increase in amplitude of excursion, heart rate and output. Eventually this stimulation may be great enough to engender cardiac irregularities. With suppression of the coffee habit, impulse formation slowly regresses. Alcohol is probably an unimportant cause.

Amphetamine is a different story. Many reducing pills contain varying amounts of amphetamine or thyroid. Being a sympathotonic drug it may be responsible for the initiation of premature systoles. A direct myocardial action may precipitate ectopic beating even in normal persons but especially in patients with heart disease.<sup>6</sup> Atrial tachycardia and atrial ectopic beats appear most frequently. When premature systoles begin to appear after large doses of amphetamine, the agent must be withdrawn.

Thyroid hormones affect the heart in a variety of ways.<sup>4</sup> There is heightened sensitivity to catecholamines, increased cardiac work and a stimulation of the sympatho-adrenal system. In consequence it may initiate formation of ectopic impulses in the atria especially since his hormone increases the basal metabolic rate in the atria more markedly than in the ventricles. Perhaps this is one reason why atrial arrhythmias predominate in hyperthyroidism. Most authors agree that underlying cardiac disease predisposes to arrhythmias associated with hyperthyroidism. This state then exhibits again the two important factors in the generation of ectopic beats, heightened sympathetic tone and an exciting agent working synergistically. If rendering the patient euthyroid is insufficient to control the ectopic mechanism, it may become necessary to employ a digitalis glycoside.

It is obvious that the recognition of the nature of the premature systole or tachycardia is predicated upon a precise diagnosis of the abnormal rhythm. If we bear in mind the interaction between the sympathetic nervous system and an exciting agent in the genesis of the ectopic impulse formation, we are in possession of the knowledge regarding the initiation of the abnormal mechanism and how best to cope with it.

As clinicians we will do well to recall MacKenzie's classic observation. "It may be stated that when the extrasystole is the only abnormal sign, the prognosis is a favorable one; and where it is associated with other signs the prognosis is to be based upon these other signs."

L.H.N.

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## Breaking The Cigarette Habit

*It's easy to quit smoking. I've done it hundreds of times.—Mark Twain*

All knowledgeable people agree that cigarette smoking is a health hazard of sufficient importance to warrant appropriate remedial action. Some such action includes efforts to prevent youngsters from taking up cigarette smoking. Some deal with



methods of helping smokers to break the habit. Regardless of whatever general educational actions may be taken to discourage the appetite for cigarettes, there remains the formidable problem of assisting individuals to stop smoking. Most smokers have had serious difficulty as did Mark Twain when he tried to stop. The reason is that smoking is a habit that is thoroughly ingrained by a lifetime pattern of behavior which is disrupted only with great difficulty. The habit appears to be as difficult to overcome as is that of over-eating or drinking to excess.

The factors which perpetuate the cigarette habit have long been debated. The consensus of scientific opinion is that true addiction to cigarettes does not occur. The Economic Research Service U.S. Department of Agriculture states "The overwhelming evidence points to the conclusion that smoking—its beginning, habituation and occasional discontinuation is to a large extent psychologically and socially determined."<sup>1</sup> However, psychological and social factors have been dealt with to a limited degree in most smoking clinics. A complete and individualized investigation of the role of these factors and the ways in which they can be modified may make possible an effective approach to treatment of the cigarette habit. For the present, the most popular techniques used to assist the individual to stop smoking are educational campaigns, psychotherapeutic measures, pharmacologic methods and combinations of these.<sup>2</sup>

As far as educational techniques are concerned it must be admitted that on the whole no important lasting change in cigarette smoking has followed attempts to stop smoking by this method. There is the Edinburgh experience where the public was informed of the hazards of smoking through paid advertisements, articles in newspapers, posters in buses and public places, pamphlets, letters from the ministry of health to every household, 94 special meetings for teachers, parents and civic organizations. A survey of people before the campaign and six months later revealed "the campaign did not increase the proportion of non-smokers in the population and the proportion of heavy smokers to non-smokers remained unchanged." The same was true after The Royal College of Physicians publicized that smoking is a cause of lung cancer, bronchitis, and probably contributes to coronary artery disease and other common diseases. Only a very small proportion of people surveyed, 6.6 per cent stopped cigarettes for at least three months.

In this country, after the publication of the U.S. Public Health report on smoking there was a sharp but temporary decline in cigarette production with a concomitant temporary increase in the production of cigars and smoking tobacco. However, there

was no important lasting change in cigarette production. The reason for the failure is evident. The story about dangers of smoking in the news media was unsustained, whereas the manufacturers continued to carry on a persistent advertising campaign.

Physicians however have had in the last decade continual exposure to reports on the hazards of smoking, have become convinced of these hazards and have themselves stopped smoking in increasing numbers. In 1954, 52 percent of Massachusetts physicians smoked cigarettes. Currently this proportion had dropped to 22.5–33 per cent. The reduction occurred slowly. Of course doctors are a unique group in that they personally observe the disability and death in their patients from diseases linked with cigarette smoking. The lesson from this is that one-time efforts will be unsuccessful whereas "long-term" campaigns can show results. This gives support to the concept that people can be persuaded to stop smoking if the hazards are presented convincingly and persistently over long periods of time.

Psychotherapeutic measures usually of a superficial type employed in most smoking clinics are generally ineffective over the long pull. This is true of the experience of the clinics held by the London Ministry of Health. Lawton<sup>3</sup> tried group psychotherapy in a group of confirmed smokers. The group met for nine 90-minute sessions over a period of six weeks. Twelve of the group stopped and eight were still not smoking three months later, but 18 months later only three were still abstaining from smoking. Hypnosis and post-hypnotic suggestion have also been used in some anti-smoking campaigns, but their efficiency has not been evaluated objectively.<sup>2</sup>

Pharmacologic methods have also been used as smoking deterrents. Anesthetic lozenges, astringent mouth washes, anti-cholinergic drugs, sedative like hydroxyzine or meprobamate and finally lobeline. None of these substances have been found to be any better than placebos.<sup>2</sup>

Because the individual treatment modalities have not been notably effective in terminating the cigarette habit, there has been a tendency to combine these treatment methods in smoking treatment clinics. Typical programs last from 10 days to six weeks, and employ education approaches, various psychological techniques, diets, exercises, tranquilizers, lobeline and other measures. Such clinics have been operating in the Scandinavian countries since 1958. They have also been established in Canada, Great Britain and other European countries and also in this country under the sponsorship of religious orders, municipalities, foundations and health agencies.



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Only in a few instances have the effectiveness of these clinics been evaluated. Of 1,012 cigarette smokers who attended the anti-smoking clinics in Stockholm,<sup>4</sup> 76 per cent of those who had completed the 10 day course of treatment said they had stopped smoking completely and an additional 22 per cent reduced their consumption to less than a quarter of the number of cigarettes smoked before treatment. Six months later it was disclosed that only 23 per cent were still abstaining from smoking cigarettes and an additional five per cent were smoking less than 25 per cent of their previous consumption. In this country no improvement over the results described have been reported.

A glance at the results shows clearly that it is the high relapse rate which is a recurrent problem in all clinics which have analyzed their long term effects. Several factors which influence the relapse rate have been identified. The relapse rate is greatest among those who merely reduce the number of cigarettes smoked, and least among those who ceased entirely. For example Lynch<sup>5</sup> found that relapse occurred within three months in 50 per cent of persons who reduced the amount of smoking or changed to cigars or pipe but only in nine per cent of those who completely stopped smoking. Similar results were reported by Hammond and Garfinkel.<sup>6</sup>

The length of time individuals have abstained from cigarettes is another important factor determining whether or not they will resume the habit. This is borne out clearly by Hammond's figures. The relapse occurred in 37 per cent of persons who had discontinued smoking for one year, in 19 per cent of those who stopped smoking for 1-2 years and only in five per cent of those who had stopped two or more years. Hammond's figures also identify three other factors as related to the relapse rate and inextricably to each other: current age, age at which cigarette smoking was started and the degree of inhalation. The risk of relapse was high in the younger cigarette smoker, the earlier age at which he started smoking and the more he inhaled.

If high relapse rates are to be avoided, the habit of "non-smoking" must be reinforced over a period of at least two years. Currently only limited assistance can be offered the individual who desires to stop or whose health contra-indicates cigarette smoking. However, experience is accumulating with a variety of non-smoking measures and these should provide a basis for further development of treatment methods.

The doctor must tell his cigarette smoking patients that one cigarette smoked takes away 14½ minutes of his life. Twenty cigarettes smoked a day takes away eight years of his life and 40 cigarettes reduces his longevity by 16 years.<sup>7</sup> Such stark real-

ism can jolt his patient in recognizing the dangers of cigarette smoking.

L.H.N.

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## Oxygen Toxicity In Hyperbarism

Man's dependence upon the earthly atmosphere is being challenged by our attempts to probe into space, by going deep under water and by attempting hyperbaric oxygenation in medicine. In each instance the effort has been to establish and maintain a life sustaining milieu independent of and isolated from the surrounding environment using oxygen as a major component. In all of these efforts a limiting factor has been man's intolerance to oxygen at high ambient pressures and concentrations. Webb, et al.<sup>1</sup> have just reported that hyperbaric oxygen tensions oxidize the pulmonary surfactant in guinea pigs and rats leading to atelectasis.

Margolis and Brown<sup>2</sup> have just reported studies on the dog exposed to hyperbaric oxygenation. With standard Navy diving and decompression techniques, they placed mature healthy mongrel dogs individually and without anesthesia or restraint in a 1 meter<sup>3</sup> chamber and exposed them to 100 per cent oxygen at three atmosphere pressure for more than four hours. The CO<sub>2</sub> produced by the animal was extracted by soda lime. Some animals developed seizures but this event did not terminate the experiment. After removal from the chamber, the animals were observed for six to thirteen days following exposure, for neurologic impairment.

The only change attributable to oxygen toxicity was a characteristically ocular lesion. This consisted of segmental degeneration of axons in the nerve fiber layer of the retina in the region encompassing and surrounding the optic nerve head. The lesions appeared identical to cytoid bodies, the microscopic

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**\* Reference:** Litchfield, H. R.: Archives of Pediatrics,  
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components of the "cotton-wool spot" which is characteristic of retinal vascular disease in man. This cytoïd lesion appeared in all 12 dogs subjected to a single hyperbaric exposure of four hours or more. It was absent in two dogs exposed for 210-235 minutes and also absent in 83 dogs that received hyperbaric oxygen for 45-120 minutes to test this procedure against the sequelae of circulatory arrest.

It has been known since the etiology of retrolental fibroplasia was established, that the immature retina is highly sensitive to the toxic action of oxygen. Recently Ashton and Pedler<sup>3</sup> demonstrated that ambient hyperoxia also exerts a selective action upon the endothelium of developing retinal vessels although it does not injure directly other retinal structure or affect immature cerebral or meningeal vessels. Noell<sup>4</sup> showed that in rabbits this sensitivity exists also in the mature eye, but with the visual cells rather than the vascular bed as the target tissue. He tested this by finding a depression of the electroretinogram (ERG) after exposure to 100 per cent oxygen at 1 atm. for more than twenty-four hours. However, when he exposed his animals to hyperbaric oxygenation, then alterations were both accelerated and intensified. Depression of the ERG was greatest after three to five hours exposure to 100 per cent oxygen at 3 atm. The injury to the visual cells became irreversible after five to six and one-half hours and frequently after shorter exposures.

The death of visual cells in rabbits as described by Noell and the segmental degeneration of nerve fibers in dogs that Margolis and Brown observed provide two different anatomical indices useful for further studies of the pathogenesis of oxygen toxicity. We know that high oxygen tensions constrict cerebral and retinal vessels and this raises the question as to whether the ocular lesions are caused by ischemic anoxia. If the blood flow is reduced by prolonged vasospastic response, is it sufficient to overcome the increased oxygen transport of hyperbarism? This question remains for further study.

There is of course another possibility, namely that the retinal injury could be due to inhibition by oxygen of membrane or intracellular enzyme reactions. This fact could account for both the death of visual cells and for segmental lesions in their processes. Oxygen at elevated pressures is a potent toxin of living cells.<sup>5</sup> When its liberation is facilitated by small amounts of CO<sub>2</sub> then neurotoxic effects such as convulsive responses, paralysis, and death are all accelerated or increased in incidence. This could hardly be due to ischemic anoxia.

Margolis and Brown were able to prevent the eye lesions by the use of 98 per cent oxygen and

two per cent carbon dioxide at 3 atm. But in these experiments there was merely a shift in the locus of the toxic action of oxygen from the eye to the central nervous system which was manifested clinically by overt neurologic deficits and histologically as selective neuronal necrosis. We thus have two separate mechanisms that may be operative in oxygen toxicity. One is increased vascular resistance induced by the hyperoxia which could result in ischemic retinal necrosis. The other is direct oxygen toxicity upon the membrane and cellular enzymes.<sup>6,7</sup>

It is very likely that the gross counterpart to the retinal injury the "cotton wool" lesion might be seen with the ophthalmoscope. In that case, it might be a useful sign of oxygen toxicity. However because the discovery of the lesion by Margolis and Brown was unexpected, they have not yet had the opportunity of observing it in the living animal.

More recently Peter, et al.<sup>8</sup> studied the effects of hyperbaric oxygenation on coronary occlusion in pigs and found that it prolonged the life of the animals only long enough to reveal the acute necrosis. No eye studies were made on the pigs. However, even if some pigs had survived the infarction, total blindness would be too great a price to pay for such doubtful benefits.

The perils to the eye posed by oxygen at high pressure are of particular significance to hyperbaric medicine and to undersea ventures. Neither can these findings be neglected by our man in space program, since prolonged exposure to oxygen at a partial pressure of over 350 mm Hg is also regularly attended by toxic manifestation.

L.H.N.

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# The Significance Of Antibody Titers and Amniocentesis In Erythroblastosis Fetalis

Maclyn E. Wade, M.D., C. D. Davis, M.D., Ernest Kohorn, M. Chir., FRCS. MRCOG.  
and Wayne Ulinik, M.D.

■ A case of Erythroblastosis Fetalis is presented to illustrate the use of amniocentesis and to support the plea that the amniotic fluid should be examined in all sensitized patients however low the antibody titer.

In 1952, Bevis<sup>1</sup> demonstrated a relation between the bilirubin content of the liquor amnii and rhesus sensitization. Walker<sup>2</sup> in 1957, found a 95 per cent correlation between the presence of bilirubin pigments in amniotic fluid and the development of erythroblastosis in the infant. In 1961, Liley<sup>3</sup> reported his experience with amniocentesis in sensitized patients and demonstrated that the size of the 450 M $\mu$  deviation of the spectrophotometric absorption curve of the liquor, provided an accurate indication of the degree of fetal hemolysis and thus of the fetal anemia. He established criteria for the management of these patients based on these findings and placed them in three groups, depending on the size of the spectrophotometric deflection, the greater deflection indicating more severe hemolysis. Depending upon the maturity of the fetus, intrauterine transfusion or premature delivery would be performed in the more severely affected cases. (Zones II and III), (Figure I).

Using these criteria Liley<sup>4</sup> reduced the perinatal mortality of Erythroblastosis Fetalis from 22 per

cent to 9 per cent and Freda<sup>5</sup> has reported similar results in New York. Up to the present amniocentesis has been performed only if the maternal antibody titer was found to be more than 1:64.

## Case Report

Mrs. C. P., a married white female age 26, G5, P 3, A 1, was referred to the Yale University Medical Center on October 12, 1965. She is group A, Rh negative and her husband is group O, Rh positive. She has had no blood transfusions.

In 1958 she had an abortion. She then had three pregnancies, in 1960, 1961 and 1963. In the first two of these pregnancies no antibodies developed but in the last pregnancy there was a titer of 1:4. The infants were delivered at term, at 37 weeks and at 38 weeks respectively. All infants were Rh positive but only in the last pregnancy was the Coombs test positive. No infants required exchange transfusion.

During the present pregnancy the LMP was 2/7/65 and the EDC 11/14/65. The pregnancy was uneventful apart from the finding of an antibody titer of 1:8 at 9 and 26 weeks. She was referred for an opinion at the 35th week of gestation. As it was felt that all sensitized patients should have an amniocentesis this procedure was performed. The optical density difference was found to be 0.18 (Figure II) placing the patient in Liley's Zone III. This implied that the fetus was in grave danger. Labor was therefore induced and the baby was delivered.

The child weighed 2745 grams. Investigation showed the cord hemoglobin was 6.8 gms, cord hematocrit 24 per cent, cord Coombs test was 4+ positive. Cord bilirubin was 14.6 mgs. per cent, direct 9.9 mgs. per cent. There were 276 nuclear red cells per 100 white cells. The reticulocyte count of the infant was 62 per cent.

Exchange transfusion was performed and the infant did well. The Coombs titer obtained from the mother on the day of delivery was 1:16.

## Comments

This case again illustrates that the antibody titer of maternal serum does not give a good indication

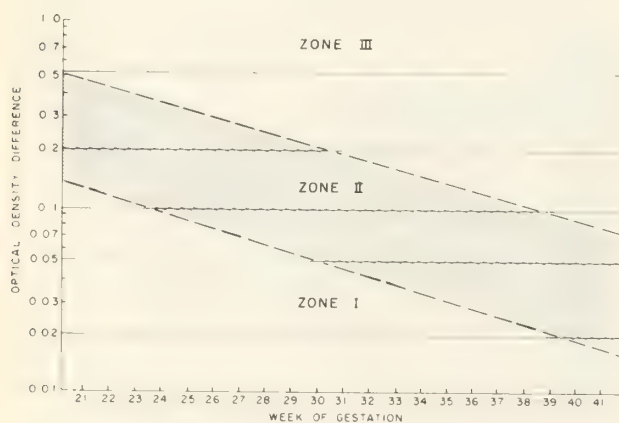


FIGURE I

From the Department of Obstetrics and Gynecology, Yale University School of Medicine, New Haven, Connecticut.

Supported by 1) General Clinical Research Grant, USPHS 3M01-FR-3805. 2) USPHS Grant 1-S01-FR-05358-04.

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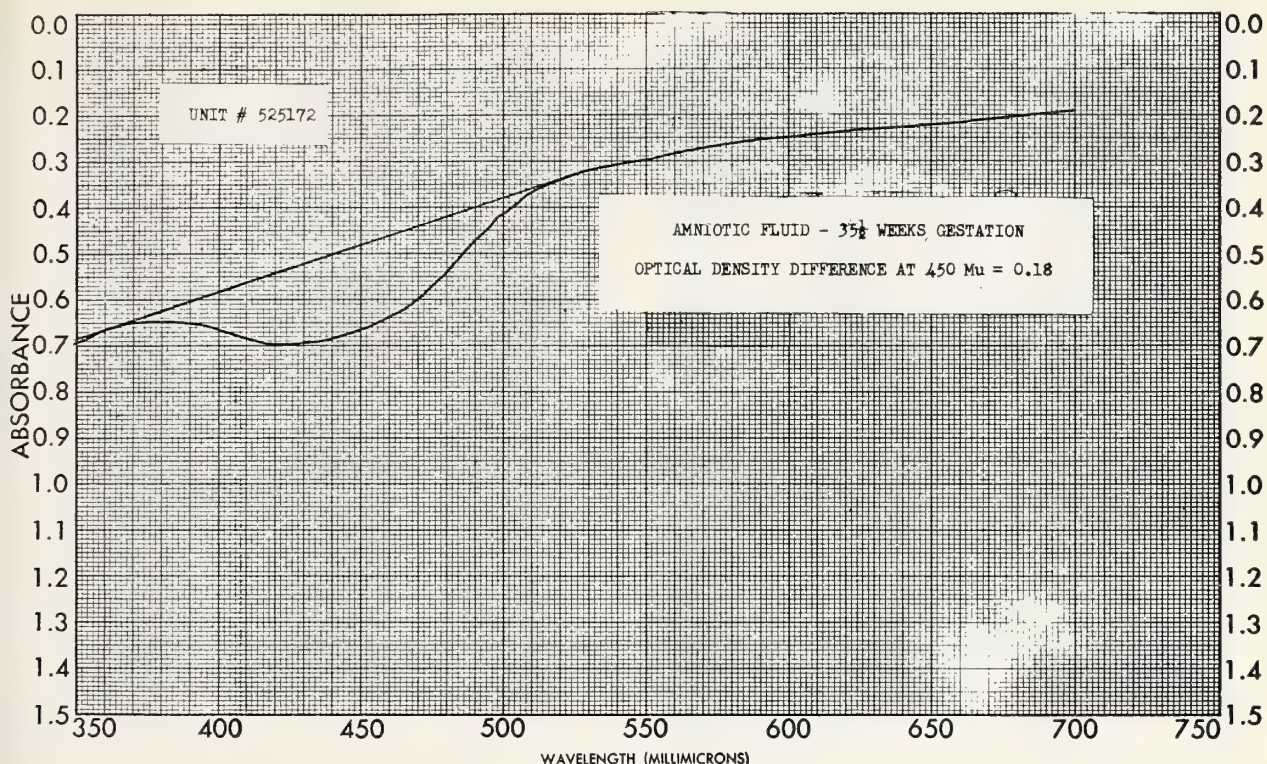


FIGURE II

of the severity of the hemolytic disease in the infant. A titer as low as 1:8 may be associated with severe disease. It is felt that amniocentesis should be performed routinely in all patients who have any antibody. Low titers may lull one into a sense of false security.

In experienced hands the procedure is relatively free from risk. In 120 amniocenteses at Yale-New Haven Medical Center there have been no complications.

It is the practice to perform the first amniocentesis at the 30th week of gestation except if the previous infant has been severely affected or there has been a previous stillbirth in which case amniocentesis is first performed at the 20th week. Repeat amniocenteses are then performed as indicated.

### Summary

A brief account of the history and significance of amniocentesis is presented. Although a rising titer gives some correlation with the severity of the ery-

throblastosis in the infant, a low antibody titer does not do so and may lull one into a false sense of security.

Amniocentesis, being relatively safe in experienced hands should be performed in all sensitized patients.

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Science, like life, feeds on its own decay. New facts burn old rules, then newly developed concepts bind old and new together into a reconciling law.

—William Jaines

# Intrauterine Fetal Transfusion – Indications And Management

C. D. Davis, M.D., Maclyn E. Wade, M.D., Ernest Kohorn, M.Chir., FRCS., MRCOG.  
and Wayne Ulisnik, M.D.

■ Liley<sup>1</sup> first reported a successful intrauterine fetal transfusion in 1963. Since then this procedure has been utilized with varying success in selected cases.<sup>2</sup> Precise clinical indications for performing the procedure are gradually evolving.

The object of this report is to discuss criteria for the selection of patients for intrauterine fetal transfusion and some of the difficulties that the management of these patients presents.

It is preferable that patients with Rhesus sensitization are seen in a special clinic so that an experienced team can deal with the problem. Spectrophotometric changes in the amniotic fluid, optical density difference at 450  $M\mu$ , reflect the degree of fetal anemia and are a practical guide for clinical management.<sup>3</sup> We do not feel, however, that one is justified in choosing a specific optical density difference, such as 0.15  $M\mu$  or 0.02  $M\mu$ , and arbitrarily state that this is the point above which all patients will be induced or transfused in utero. This conclusion is based upon the fact that the significance of a specific optical density difference changes as the length of gestation increases. (Fig. I).

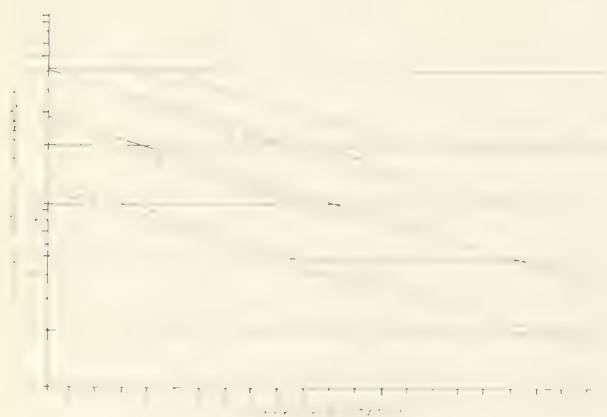


FIGURE I

Modified from Liley<sup>1</sup> and extrapolated from 27 weeks to 20 weeks of gestation.<sup>3</sup> Zone I—Fetus mildly affected or unaffected. Zone II Fetus moderately to markedly affected. Zone III Fetus severely affected.

From the Department of Obstetrics and Gynecology, Yale University School of Medicine, New Haven, Connecticut.

Supported by 1), General Clinical Research Grant, USPHS 3 MO 1-FR-3805; 2), USPHS Grant 1-SO1-FR 05358-04.

All sensitized patients should have an amniocentesis, however low the anti-Rh titer<sup>4</sup> may be. If the patient has a history of previously severely affected infants or has a high anti-Rh titer early in pregnancy, the first amniocentesis should be performed at or near the 20th week of gestation. The result obtained from this initial investigation will serve as a guide to the timing of further amniocenteses. In this way serial optical density differences will be obtained, and if the pattern indicates a rapid increase to upper Zone II or Zone III, there should be no doubt that the fetus is severely affected.

If the fetus is felt to be in jeopardy and if the estimated fetal weight and the gestational age are not sufficient for safe premature delivery, then intrauterine fetal transfusion should be considered. A history of previous stillbirths due to erythroblastosis fetalis or a repeated neonatal exchange transfusion would sway us toward performing a transfusion in utero.

Experience indicates that the markedly hydropic fetus is unlikely to survive, however successful the transfusion may be technically. Infused red blood cells are not absorbed readily from the fetal peritoneal cavity in the presence of ascites. This finding is supported by other investigators.<sup>2,5</sup> The presence of ascites or scalp edema is readily visualized radiologically if 30 M Sodium diatrizoate is instilled into the amniotic cavity prior to the performance of an intrauterine fetal transfusion. If marked ascites is present we do not proceed with the transfusion. (Fig. II).

Two patients are presented as examples.

C. M., #B5-58-41, is a 21-year-old Gravida 4, Para 3, married negro female. The patient had never received a blood transfusion. Her blood group is O and she is Rhesus negative, (Anti-D). Her husband is Rhesus positive.

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The patient's first pregnancy, in 1960, resulted in a group O, Rhesus positive infant. The cord Coombs test was negative. During her second pregnancy in 1962, her anti-Rh titer rose to 1:512. At delivery the cord Coombs test was 4+ positive. The infant required two exchange transfusions. The third pregnancy in 1964 was terminated at 37 weeks' gestation by induction. The infant was Group O, Rhesus positive. The cord Coombs test was 4+. The baby required one exchange transfusion. All babies survived.

The patient's last menstrual period was 3/10/65 and her expected date of confinement was 12/17/65. The patient was first seen in the obstetrical clinic at 27 weeks' gestation. At that time her anti-Rh titer was 1:2048 and remained at this level throughout the pregnancy. An amniocentesis revealed an optical density difference of 0.17 at 450  $M\mu$ . At 28 weeks this remained unchanged. It dropped to 0.13 during the 31st week and then rapidly rose to 0.18  $M\mu$ . at the 32nd week (Fig. III). This difference placed the fetus on the borderline of Zone II and Zone III. An intrauterine fetal transfusion, using the Liley method, with modifications previously described,<sup>6</sup> was performed. The infant received 120 ml. of packed, washed, group O, Rhesus negative red blood cells. The patient was given prophylactic systemic penicillin 600,000 units IM. B.I.D. and streptomycin .5 grams IM. B.I.D. Amniocen-

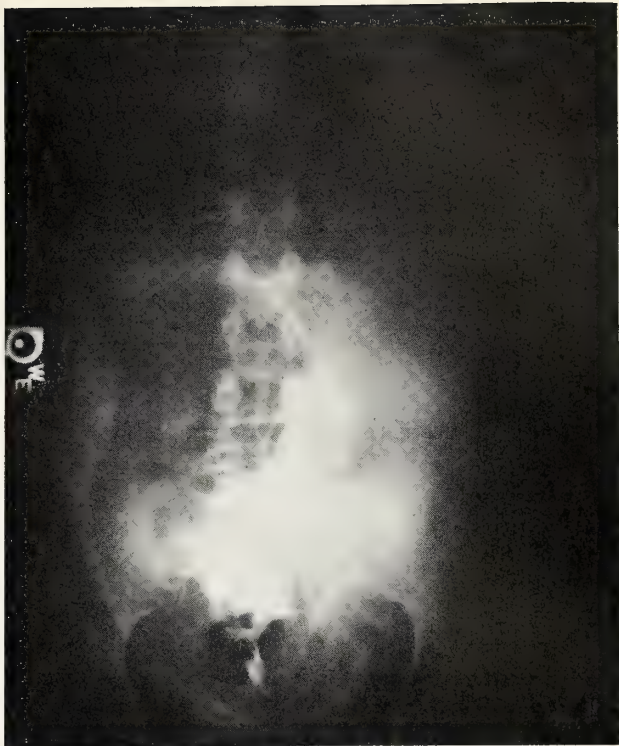


FIGURE II

Anterior-Posterior Film. 30 m. of 30 M. Sodium Diatrizoate injected into Amniotic Cavity and 3 ml. into the Fetus to outline fetal peritoneal cavity. Note marked ascites as well as scalp edema.

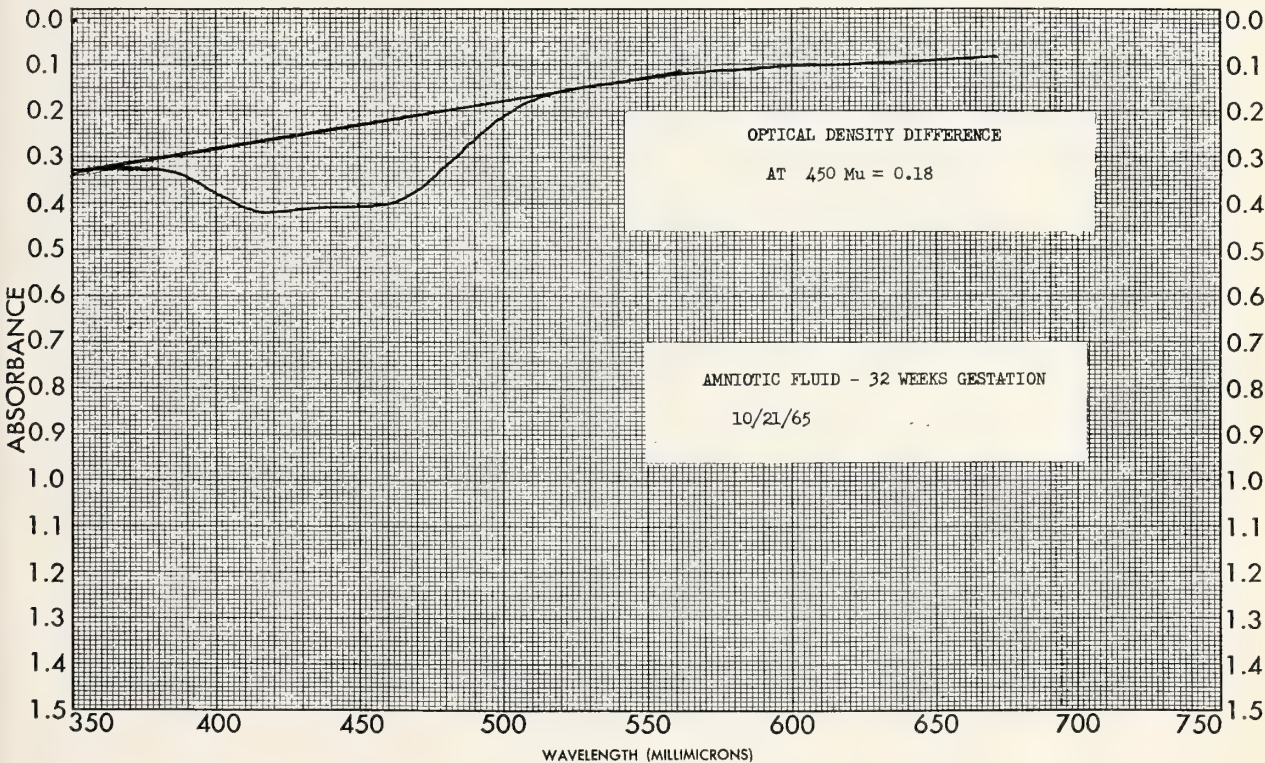


FIGURE III

Spectrophotometric curve of Amniotic fluid (C.M.) at time of intrauterine fetal transfusion.



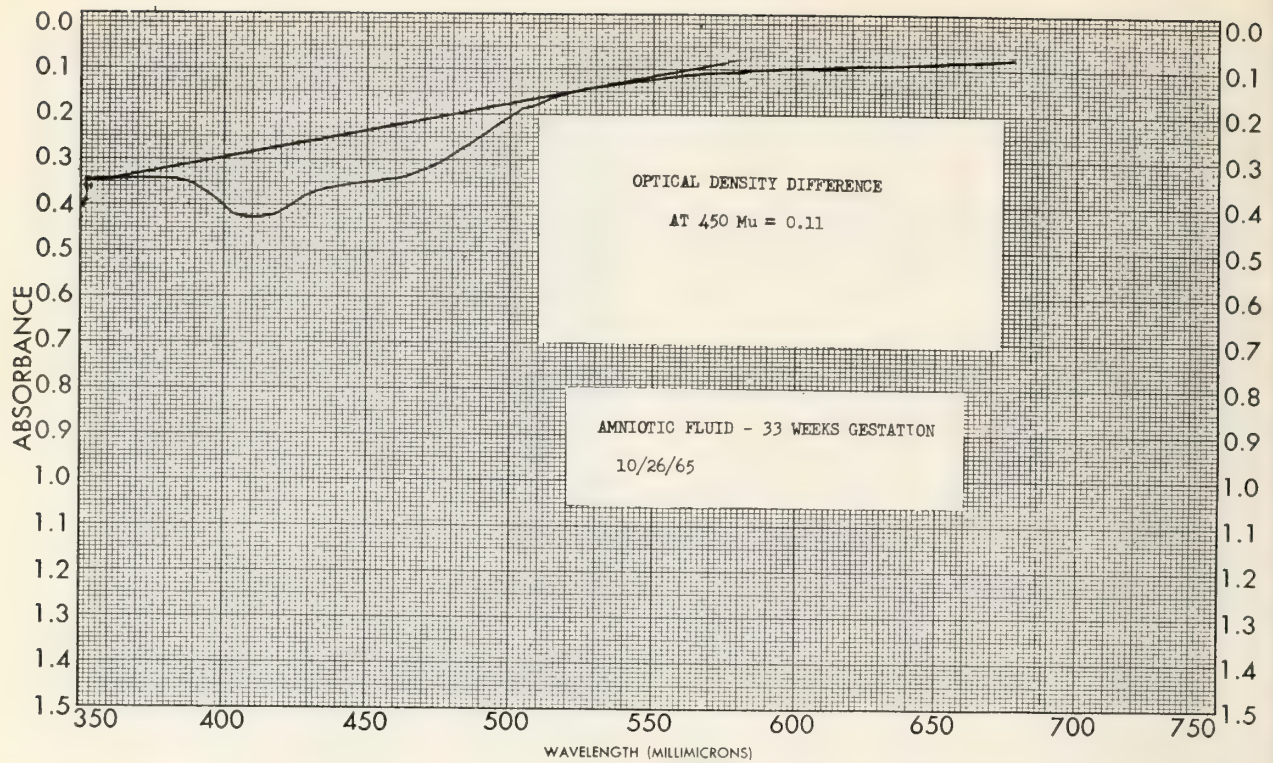


FIGURE IV  
Spectrophotometric curve of amniotic fluid (C.M.) five days after intrauterine fetal transfusion.

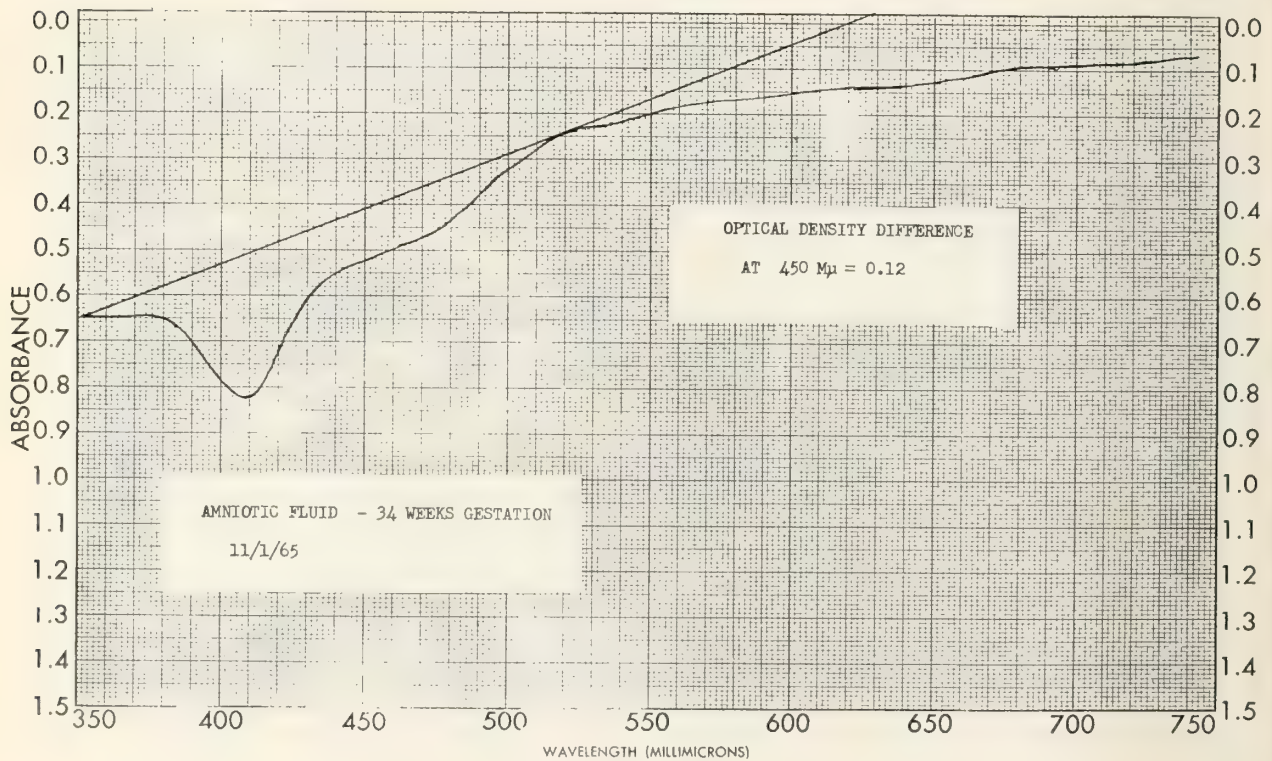


FIGURE V  
Spectrophotometric curve of amniotic fluid (C.M.) 11 days after intrauterine fetal transfusion.



tesis during the 33rd week showed an optical density difference of 0.11  $M_{\mu}$ . (Fig. IV). In the 34th week it was 0.12  $M_{\mu}$ . (Fig. V). Both these readings are in upper Zone II (Fig. VI). At that time it was felt that the fetus weighed 2500 grams and could survive early delivery. Ultrasonic measurement of the fetal head supported our clinical estimation.

The patient delivered a 6 pound male fetus. The baby was edematous and the Apgar score was 1. An exchange transfusion was carried out immediately, but despite this and vigorous resuscitation the infant died. The placenta was grossly enlarged and edematous. The cause of fetal death was congestive cardiac failure secondary to anemia. Laboratory data showed that the cord Coombs test was 4+ and the cord hemoglobin was 4 grams. Estimation of fetal and adult hemoglobin by alkali denaturation of the cord blood showed that only 10 per cent of the infant's cord blood was fetal in origin. Postmortem examination revealed the infant to be markedly edematous. Massive ascites and pleural effusions were found. The liver and spleen were enlarged three times normal size. There was no evidence of internal trauma from the intrauterine transfusion technique.

B. M., #65-38-10, is a 27-year-old Gravida 5, Para 4, married white female. The patient's blood Group is A, Rhesus negative (Anti-D). Her husband is Group A, Rhesus positive. The patient received a blood transfusion 7 years ago for postpartum hemorrhage following her first pregnancy. She had full term deliveries in 1958 and 1959. Both children were Rhesus positive. In 1960 a stillborn infant was delivered. The intrauterine demise was felt to be secondary to erythroblastosis fetalis. In 1961 the fourth pregnancy was terminated by a cesarean section at 36 weeks' gestation. The infant was exchange transfused twice and died soon after the second transfusion.

The patient's last menstrual period was 3/14/65 and her expected date of confinement was 12/21/65. The patient's anti-Rh titer remained 1:128 throughout the pregnancy. She was referred to our clinic at 32 weeks' gestation because amniotic fluid analysis had shown an optical density difference of 0.17  $M_{\mu}$  at 450  $M_{\mu}$ . Amniocentesis was repeated and the difference was 0.13  $M_{\mu}$ . It would have been helpful if samples of amniotic fluid had been obtained earlier in the pregnancy, and preferable if they had been examined in the same laboratory for a more definitive comparison. Nevertheless, both determinations placed the fetus in the upper half of Zone II.

Since the patient had previously lost two babies from erythroblastosis fetalis, the optical density difference at 32 weeks' gestation indicated a marked anemia in the fetus and the fetus was too pre-

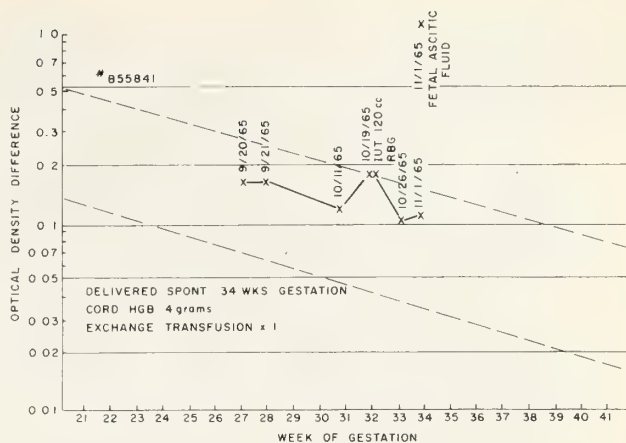


FIGURE VI

Summary of Spectrophotometric analysis of amniotic fluid (C.M.). Note: Spectrophotometric analysis of ascite fluid obtained from fetus after birth had an optical density difference of 1.0.  $M_{\mu}$ .

mature to survive early delivery, an intrauterine transfusion was performed. The infant received 100 ml. of group O, Rhesus negative, washed, packed red blood cells, hematocrit 90 per cent. Four days later, analysis of the amniotic fluid showed an optical density difference of 0.17  $M_{\mu}$ . Nine days later it fell to 0.06  $M_{\mu}$ . (Fig. VII, VIII, IX). Since our previous experience, as well as that of other investigators,<sup>7</sup> indicated that one cannot rely upon the optical density difference determinations following intrauterine transfusion, we elected to retransfuse the infant. This was performed at 34½ weeks' gestation, at which time 110 ml. of Group O, Rhesus negative, washed, packed red blood cells, hematocrit 92 per cent were instilled into the fetal peritoneal cavity. At 36 weeks' gestation the estimated fetal weight was 6 pounds. Ultrasonic cephalometry confirmed this impression.

On 11/21/65 the mother was induced and delivered of a viable 6 pound male fetus, at the Westerly Hospital, Westerly, R. I. The Apgar score was 10-10. Analysis of the cord blood showed that the fetus was Group A, Rhesus positive. The cord hemoglobin was 18 mg. and the cord bilirubin was 3.75 mg. per cent. Estimation of fetal and adult hemoglobin by alkali denaturation tests revealed that the cord blood contained 2.1 per cent fetal hemoglobin and 97.9 per cent adult hemoglobin. Optical density difference of the amniotic fluid obtained at delivery was 0.09  $M_{\mu}$ . The infant has done well.

### Comments

Both these patients had intrauterine fetal transfusions that were successful as shown by lack of trauma to either fetus, and by the presence of 90



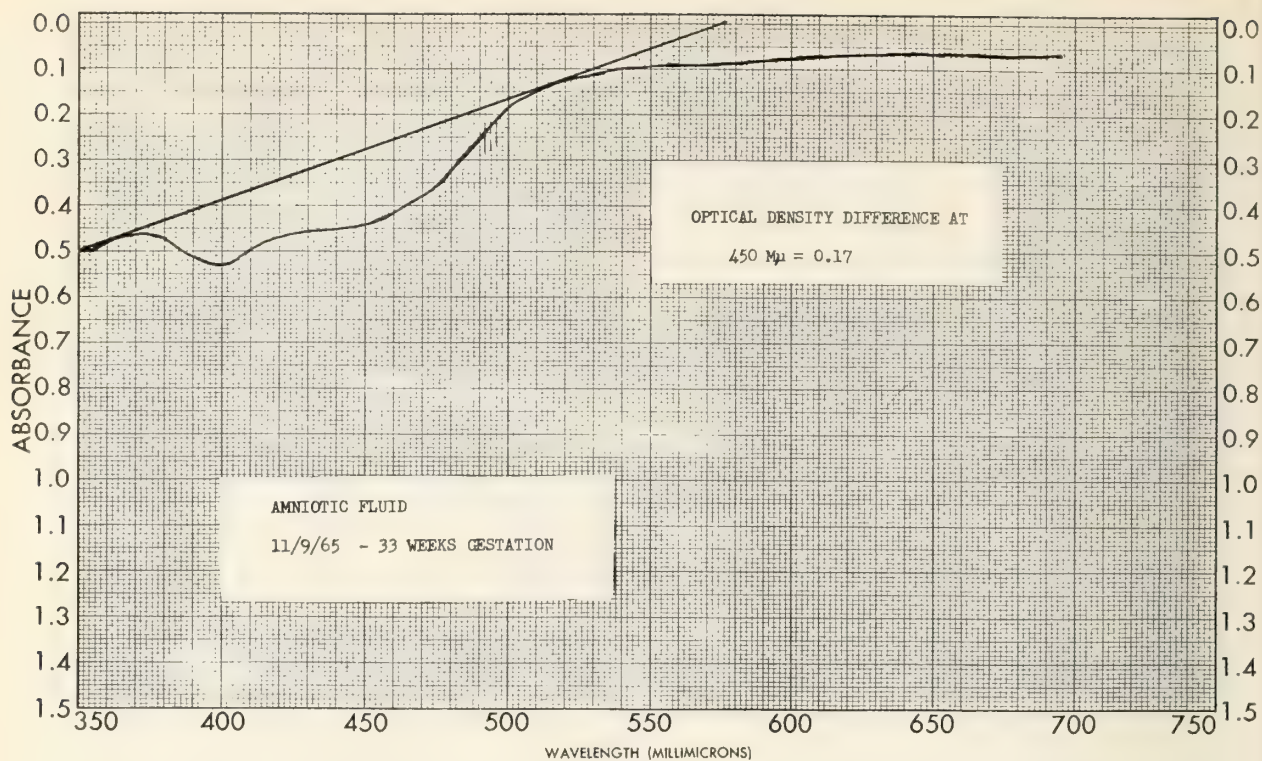


FIGURE VII

Spectrophotometric analysis of amniotic fluid (B.M.) obtained four days after the first intrauterine fetal transfusion.

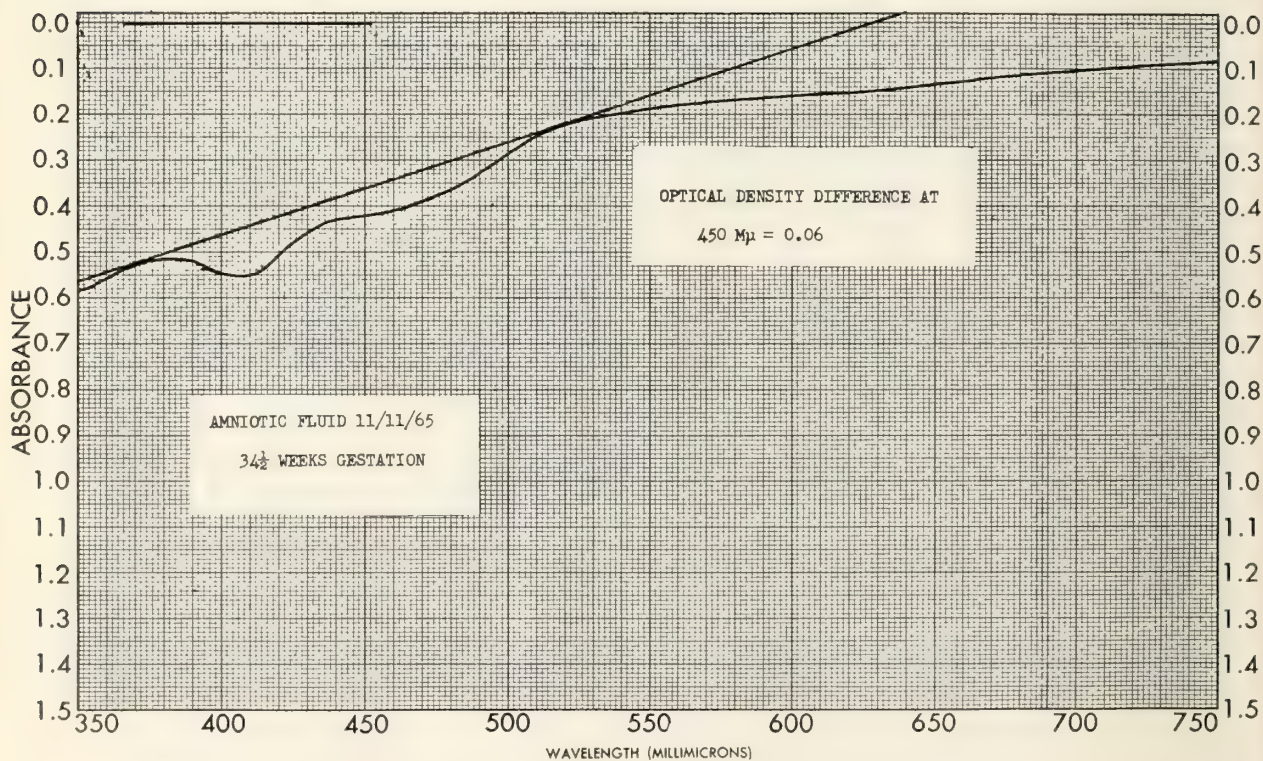


FIGURE VIII

Spectrophotometric analysis of amniotic fluid (B.M.) obtained 13 days after the first intrauterine fetal transfusion.



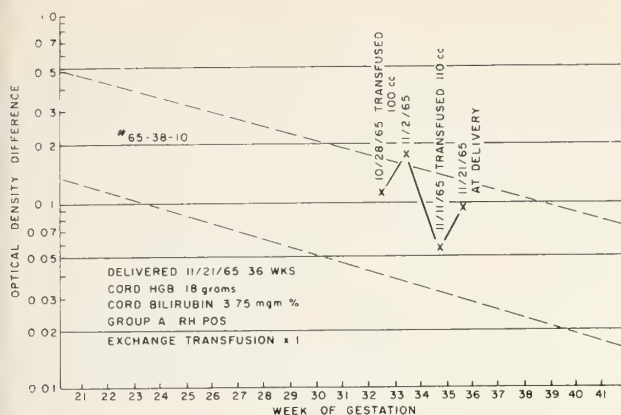


FIGURE IX

Summary of Spectrophotometric analysis of amniotic fluid (B.M.).

per cent or more adult red blood cells in the cord blood. The first patient demonstrates that the determination of the optical density difference at  $450\text{ M}\mu$  by spectrophotometric analysis of the amniotic fluid after intrauterine transfusion may be misleading. The two lower readings following fetal transfusion lulled us into a false sense of security. This experience indicated that these fetuses should be re-transfused, either weekly or every ten days, even if the optical density difference of the amniotic

fluid has decreased. Freda's<sup>7</sup> experience has led him to the same conclusion. Re-transfusion was performed with good effect in the second baby.

### Summary

1. Criteria for selecting candidates for intrauterine fetal transfusion are presented.
2. Two cases of intrauterine transfusion and the problems inherent in their management are discussed.

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I cannot conceive of the practice of medicine in which there is any breach of absolute trust and confidence between patient and doctor. A good physician cannot lie to his patient. If the truth be bitter he must help the patient face it. On the other hand, I could not bear the practice of medicine if I felt obliged to tell the patient everything I know or think I know . . . In a materialistic age in a society which certainly is not notable for individual bravery, independence of thought or a philosophic attitude, it will not be possible to make a philosopher out of every man during a terminal illness. Perhaps Sir William Jenner's three essential qualities for the Medical Man will see us through such difficult times: "He must be honest, he must be dogmatic, he must be kind."

—William B. Bean, "On Death."

# Wilson's Disease Presenting As Pancytopenia: Splenectomy In Management

Harvey W. Kaetz, M.D., Stanley S. Brodoff, M.D. and Anthony W. Robbins, B.A.

## Case Report

■ Primary splenic pancytopenia is considered by many to be a true entity.<sup>1</sup> However, most observers feel that it is not a primary syndrome, but a manifestation of illness that is obscure for want of better diagnostic techniques or keener observation, perhaps more often the latter.

We recently had the opportunity to observe a young girl who was referred to one of us by her physician,\* because of anemia and splenomegaly, and her illness is an illustration of the need for keener observation.

Miss C. P. (YNHH #63-55-81) was a 15 year old white girl who sustained a back injury while playing soccer at school in September 1964.

Further history revealed that she had been found to be anemic in a routine school survey in June of 1963, but this was not investigated. For the past two years she had noted frequent nosebleeds and bleeding of her gums with brushing but since early January of 1965, nasal and gingival bleeding had been spontaneous. She had not yet begun to menstruate.

Her past history was not contributory. There had been no known exposure to chemicals or drugs. The family history was not significant. Her father, age 44, and her mother, age 39, were in good health. She had one sister, age 13, who was well. A paternal aunt had died of diabetes at age 45; a paternal grandfather had died of cancer of the stomach. There was no family history of anemia, jaundice, or splenomegaly.

At examination on January 26, 1965, her height was 68 inches and her weight 121 pounds. Her blood pressure was 120/50; temperature, pulse and respirations were normal. The patient was a pleasant, cooperative white girl with facial and mucous membrane pallor. Questions were answered slowly and with a slight tendency to slur some words. It was noted that she took a full 10 minutes to get undressed for examination but at the time, little emphasis was attached to these observations. There was fresh gingival bleeding as well as old small clots. There were scattered fresh ecchymoses over the thighs. The spleen was huge, firm, and

non-tender. It filled the entire left upper quadrant of the abdomen, extending 4 inches below the left costal margin. The liver was not palpable. There was no adenopathy. There were two small spider angiomas on the left hand. There was no jaundice of the skin or sclerae.

Hemoglobin was 10.4 grams per 100 ml., red cell count was 3.82 million per cu. mm., white cell count was 2900 per cu. mm. with 40 per cent neutrophils, 16 per cent band forms, 35 per cent lymphocytes, 4 per cent monocytes, 3 per cent atypical lymphocytes, 2 per cent eosinophiles. Platelet count was 72,000 per cu. mm.; hematocrit was 34 per cent. On the stained smear, the red blood cells looked normal but the platelets were diminished.

She was admitted to Yale New Haven Hospital on February 10, 1965 with a diagnosis of splenomegaly with pancytopenia, etiology unknown and ? neurologic disease. On admission, the hemoglobin was 9.2 grams per 100 ml., the hematocrit was 28 per cent, the white blood cell count was 2300 per cu. mm. with 29 per cent neutrophils, 16 per cent band forms, 1 per cent eosinophiles, 40 per cent lymphocytes, 8 per cent monocytes, 3 per cent basophiles, and 3 per cent atypical lymphocytes. On the stained blood smear, platelets were considered reduced in number, and poikilocytosis, anisocytosis, and hypochromia were considered slight. Some giant platelets were noted. The platelet count was 15,000 per cu. mm.

The day after admission, the medical assistant resident\*\* noted that the patient had Kayser Fleischer rings. He had first thought her eyes were brown but then noted that the patient actually had blue irises, covered peripherally by large brownish corneal rings. It then became apparent that the dysarthria and dystonia, ignored on previous examination, were significant. Observation of the patient

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also showed a somewhat fixed facial expression with a constant small smile and an open mouth.

Further laboratory studies showed a ceruloplasmin of 17 units, total bilirubin of 1.26 mgm. per cent, cephalin flocculation of one plus in 48 hours one one occasion and of four plus in 48 hours on another. One prothrombin time was 40 per cent of normal but several others were normal. Other liver function tests were normal. Coomb's tests, both direct and indirect, were normal. Serum electrolytes, proteins, blood urea nitrogen, blood glucose, serum uric acid, VDRL, and multiple urine tests were within normal limits. The patient's blood type was B, Rh positive (D). Hemoglobin electrophoresis showed 97.5 per cent hemoglobin A, 1.9 per cent hemoglobin A<sub>2</sub>, 0.6 per cent hemoglobin F.

A bone marrow aspiration from the posterior iliac spine on February 11, 1965 showed a normal cellular marrow with normal maturation of the white blood cell series but with normoblastic hyperplasia of the red cell precursors. Megakaryocytes were normal in number and kind. No abnormal cells were seen.

On February 16, 1965, an upper gastrointestinal series showed esophageal varices. On the same day, Dr. Stuart C. Finch, using the method of Iio and Wagner,<sup>2</sup> employed I 131 labeled aggregated albumin to demonstrate the hypersplenism. Monitoring the uptake of this material over the spleen and liver, it was shown that the spleen to liver uptake ratio was 2 to 1 as compared with the usual 1 to 2 to 1 to 5 ratio, seen in the normal patient.

In view of the above-noted findings, but particularly because of the thrombocytopenia, which was felt to be potentially lethal, it was decided that the patient should have the benefit of splenectomy. The disparity between the portal hypertension and the fairly normal liver function test profile was noted but it was decided pre-operatively that a shunt procedure would not be attempted. The reasons for this latter decision were (1) the uncertain prognosis of the Wilson's disease and (2) the effect on liver function of prolonged anesthesia and surgery.

The patient went to surgery on February 17, 1965. Anesthesia was with cyclopropane and pentothal, aided by succinyl choline and curare. A huge smooth spleen was found. There were no perisplenic adhesions. The liver was seen to have a coarse granular surface and was much reduced in size. The splenic vein was estimated at 3 cm. in diameter, and was tense with blood. The spleen was delivered into the wound and removed without difficulty. There was continuous oozing of blood in the splenic bed throughout the procedure, however, and this was controlled with surgicel. A small liver biopsy was obtained from the right lobe. Two units of

fresh blood and two units of bank blood were given during a three hour procedure. The patient left the operating room in good condition and was kept in the recovery area until consciousness returned.

The pathologic findings were as follows:

*Gross:* A huge red brown spleen 21 cm. in diameter by 17 cm. by 8 cm. containing approximately 300 cc of clotted blood. Its weight was 1162 Grams. The cut surface was firm and maintained its shape readily. Malpighian corpuscles were prominent; the sinusoids were congested and considerable blood exuded from the cut surface.

*Microscopic:* Spleen of hypersplenism, with dilatation and congestion of sinusoids, thickening of the cords of Billroth and reticulo-endothelial proliferation. The red pulp to white pulp ratio was markedly increased. Touch preparations revealed red blood cells and platelets within the reticuloendothelial cells.

The liver biopsy showed distortion of the normal lobular pattern by scar tissue and glycogen vacuolization of nuclei. There was periportal and fine perinodular scarring characteristic of early cirrhosis. There was a zone of superficial atrophy and bile duct proliferation beneath Glisson's capsule.

There was a gratifying hematologic response to splenectomy. On Feb. 17, 1965, immediately after surgery, the platelet count was 39,000 per cu. mm., on Feb. 19, 92,500 per cu. mm., on Feb. 20, 157,000 per cu. mm., on Feb. 21, 182,000 per cu. mm., on Feb. 22, 230,000 per cu. mm., on Feb. 24, 330,000 per cu. mm.

Post-operative convalescence was uneventful except for an atelectasis of the lower lobe of the left lung with an associated fever for the first three post-operative days. She was discharged from the hospital on Feb. 26, 1965.

On March 19, 1965, the patient was seen in the office. There had been no further nasal or gingival bleeding and no ecchymoses. She looked happy and seemed more vigorous and alert. The color of the skin and mucosal surface was normal. Speech was still slow with a ? scan but not different than during her hospitalization. The hematocrit was 37 per cent, the platelet count, 340,000 per cu. mm., the white count, 7000 per cu. mm. with 27 per cent neutrophils, 27 per cent lymphocytes, 16 per cent monocytes, 5 per cent basophiles, 25 per cent eosinophiles. The red cells and platelets were normal on the smear but for rare target cells and moderate anisocytosis. The eosinophilia was felt to be due to splenectomy. The prothrombin time was 100 per cent of normal. She was referred for therapy with chelating agents to the Yale University Medical School Pediatric Study Unit.

## Discussion

Splenomegaly is considered the most common sign of hepatic disease in Wilson's disease. Silverberg and Gelles<sup>3</sup> reported nine cases with splenomegaly. Boudin<sup>4</sup> also noted this, reporting five cases with hepato-splenomegaly without other signs of hepatic failure. Our case offers emphasis to the fact that portal hypertension is a major expression of liver involvement in Wilson's disease and illustrates how extreme splenomegaly may become without laboratory evidence of hepatic failure.

Scheinberg and Sternlieb<sup>5</sup> state that "hyper-splenism as manifested by thrombocytopenia may be the first symptom of Wilson's disease which brings the patient to the physician." However, the literature offers very few examples of this type of presentation. Of 14 cases of Wilson's disease that Scheinberg and Sternlieb described, only one case presented with thrombocytopenia. Silverberg and Gelles<sup>3</sup> also reported one such case. In the monograph on Wilson's disease by G. Boudin and B. Pepin,<sup>6</sup> there is recognition of the occurrence of pancytopenia and splenomegaly and one case is cited with correction by splenectomy. A survey of other data reveals no mention of this mode of onset.<sup>7-9</sup> An increased awareness of this relationship of splenomegaly, pancytopenia and Wilson's disease may reduce the "incidence" of "primary" splenic pancytopenia. A simple but informed glance at the cornea in a patient with splenomegaly and a cytopenia may pay unexpected returns. The chelated copper rings of Kayser Fleischer are reliably and specifically diagnostic when present, and if absent, laboratory tests of aid in the diagnosis of Wilson's disease should be performed.

The literature suggests that surgery and anesthesia are hazardous in Wilson's disease. Neurologic symptoms are said to be precipitated or aggravated by surgery and anesthetics are said to be poorly tolerated.<sup>8</sup> Rabiner et al.<sup>10</sup> reported two cases in which splenectomy was done because of anemia and purpura in which Wilson's disease "developed post-operatively." Boudin et al.<sup>4</sup> report a case of a nine

year old boy with hepato-splenomegaly and a bleeding tendency in whom neurologic findings appeared post-splenectomy. It would seem possible that the diagnosis was missed or not yet apparent pre-operatively in these cases. Our obviously limited experience is at variance with these reports. Our patient had no worsening of her neurologic symptomatology after surgery; nor was there any intolerance to anesthesia with the agents used.

## Summary

A 15 year old white girl with Wilson's disease is described. Her illness is of interest because of its unusual presentation with splenomegaly and pancytopenia. Surgery, with the removal of a huge spleen, was well tolerated.

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# Lingual Thyroid—A Review

Manny Myerson, M.D., and Howard W. Smith, M.D.,

## Introduction

Physicians examining the mouth should be cautious about advising removal of cyst-like masses located in the posterior one-third of the tongue. Surgeons in the various specialties should exercise caution in the removal of the cyst-like tumors, since such removal may deprive the patient of his only functioning thyroid tissue. The lingual position of the normal thyroid results from a failure of the embryonic thyroid anlage to descend from its site of origin at the base of the tongue to the normal position in the lower cervical area.

The incidence of this abnormality is low, with about three hundred reported cases in the literature.<sup>1</sup> The first reported case was in 1869 by an English physician<sup>2</sup> who reported a death by suffocation in a newborn infant, found to have a large tumor at the base of the tongue. The Lahey Clinic reported only three cases in a study of twenty-five thousand goiters up to 1947.<sup>3</sup> Since the use of radioactive iodine ( $I^{131}$ ) for evaluation of thyroid disorders after 1948,<sup>4,5</sup> an increased number of lingual thyroids have been reported.

## Embryology

The earliest pharyngeal derivative to appear in the embryo is the thyroid gland.<sup>6</sup> A median prominence arises from the floor of the pharynx between pharyngeal pouches I and II about the fourth week. This prominence develops into a vesicle with a constricted hollow stalk, the thyroglossal duct. The vesicle becomes solid and enlarges caudalward as a bilobed mass. The duct, though it may persist, usually atrophies during the fifth week isolating the gland from its site of origin at the foramen cecum. By the seventh week, the thyroid lies at the level of the laryngeal primordium. Colloid is acquired in the second month, and the characteristic thyroid follicles become established during the fourth month.

Ectopic thyroid gland may occur at any point along the descent of the primordium. The resulting locations of these glandular masses are designated as lingual, sublingual, pretracheal (normal), and substernal (Fig. 1). Small areas of functioning thyroid tissue along the thyroglossal duct tract are

fairly common.<sup>7</sup> Larger masses of thyroid tissue at the base of the tongue may remain in addition to a normal cervical thyroid. In seventy per cent of cases of lingual thyroid, however, there is no cervical thyroid present.<sup>8</sup>

The parathyroids, derived from pharyngeal pouches III and IV, have a contiguous but different origin from the thyroid. Reports of parathyroid glands in lingual thyroids have been uncertain because of the histologic similarity of parathyroid and early thyroid tissue.<sup>9</sup> In general, the complete removal of a lingual thyroid does not remove all parathyroid tissue. Asch,<sup>10</sup> however, reported the development of postoperative tetany in a case of complete lingual thyroidectomy. Microscopic sections of this thyroid showed epithelial bodies resembling parathyroid tissue.

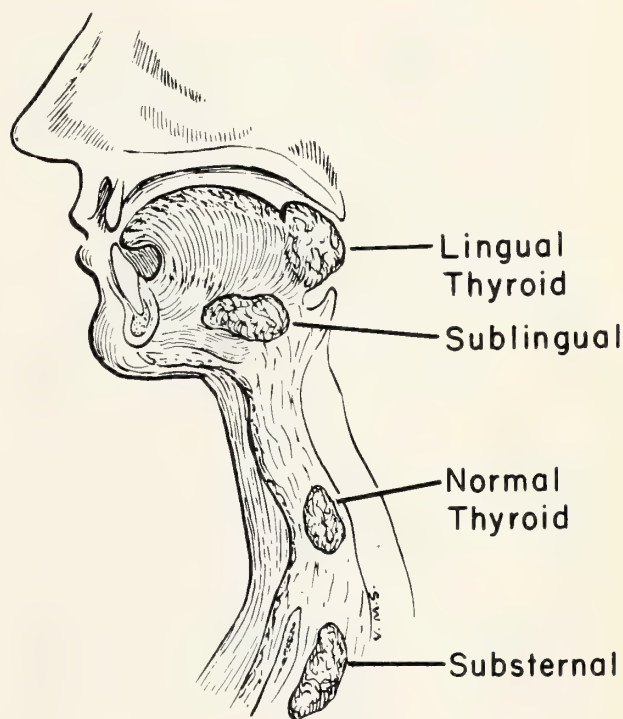


FIGURE 1

Ectopic thyroid may be found along the path of the gland's descent.

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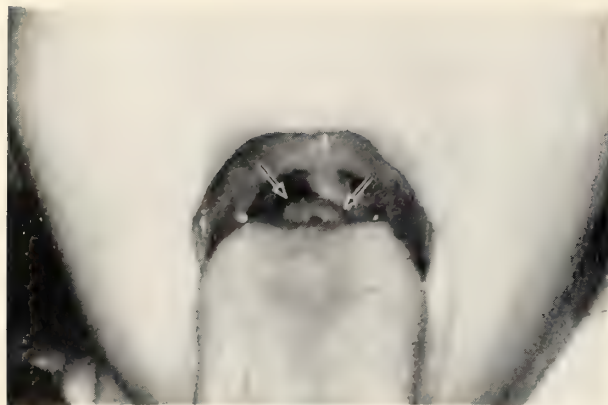


FIGURE II

Lingual thyroid in a five year old girl (arrows).

### Diagnosis

The condition may be discovered unexpectedly during a routine physical examination of the mouth and throat. Common symptoms include varying degrees of dysphagia, dysphonia, and dyspnea. Exsanguinating hemorrhage from an ulcerated lingual fetal adenoma has been reported in a patient who was presumed to have upper gastrointestinal bleeding.<sup>11</sup>

Lingual thyroids are reddish globular masses of variable size located in the median line of the base of the tongue between the foramen cecum and the epiglottis. The covering membrane is thin and glistening, and nets of overlying large veins are common. The mass may be smooth or lobulated, intact or ulcerated, and firm or soft in texture. Some are superficial with a broad base, while others penetrate deep into the tongue. To avoid the possibility of missing such a lesion, the examiner should instruct the patient to forcefully protrude his tongue. Examination with a laryngeal mirror may be helpful. One cannot be certain by palpation whether cervical thyroid is also present.

Feitelberg in 1948 first reported the use of radioactive iodine scintigrams for the study of thyroid disease and in the demonstration of lingual thyroid. A tracer dose of  $I^{131}$  is administered orally, a Geiger counter is used to tabulate the counts in the neck region, and the total uptake of  $I^{131}$  is thus estimated. The scintigram will show the presence or absence, the size, and the distribution of thyroid tissue. It is, therefore, useful for identifying as thyroid tissue a mass at the base of the tongue and in determining whether or not any thyroid is present in the neck (Figs. II-IV). Prior to the use of  $I^{131}$ , surgical exploration of the pretracheal area was necessary to establish the presence of cervical thyroid. Palpation of the anterior cervical area for thyroid gland may be misleading. Cases have been reported in which lateral lobes of the pretracheal

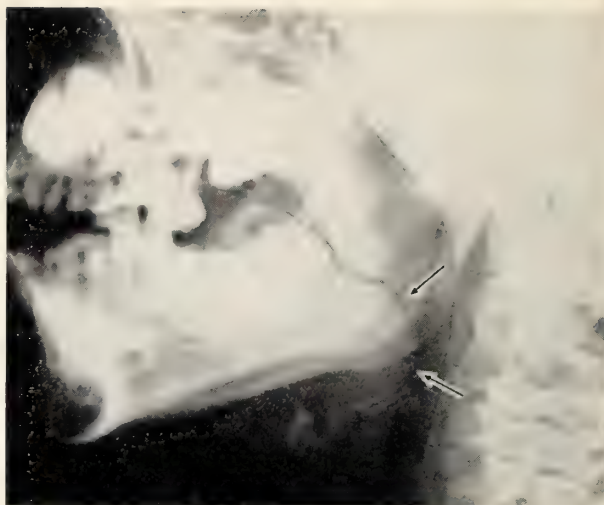


FIGURE III

Lateral X-ray of the nasopharynx shows the mass at the base of the tongue (arrows).

thyroid were mistakenly thought to be present by palpation.<sup>12</sup>

The scintigram cannot be used for definitive diagnosis of thyroid disease. In the neck, for example, one cannot distinguish by scintigram between a colloid cyst and a metabolically inactive

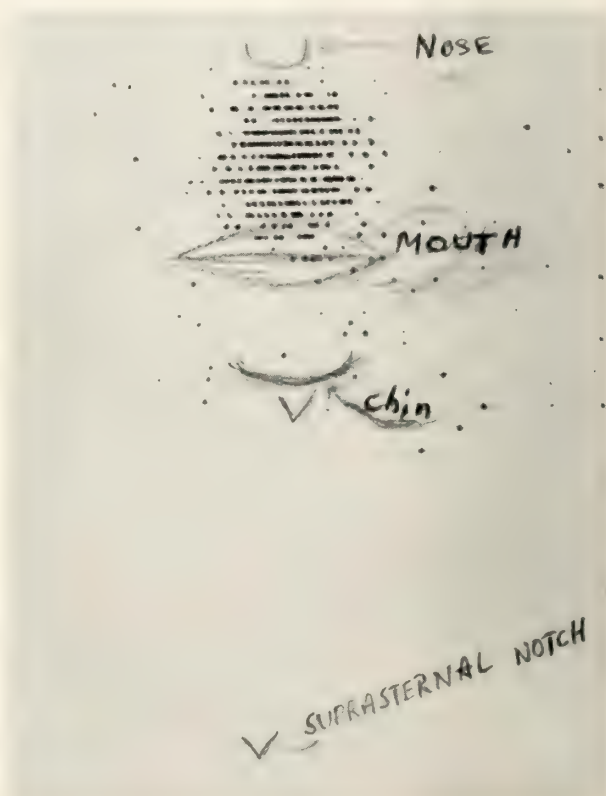


FIGURE IV

$I^{131}$  scintigram in this girl shows a superiorly located thyroid pattern with absence of activity in the cervical region.



carcinoma or between an adenoma and a metabolically active carcinoma. It would also be possible for an inactive tumor to be hidden by normal thyroid gland.

The incidence of benign non-thyroid lesions at the base of the tongue is small. Possibilities include non-thyroid cysts, adenomas, angiomas, and ectopic salivary tissue. Rarely will sarcoma or carcinoma be present here. Lingual thyroids may be mistaken for thyroglossal duct cysts, with excision causing unexpected postoperative myxedema.<sup>13</sup>

### Pathology

Histologically, the lingual thyroid glands which have been biopsied or removed have demonstrated many of the changes seen in the normally placed thyroid gland. These changes have ranged from normal thyroid tissue to hyperplasia, simple colloid goiter, adenomas, Hashimoto's disease, and rarely carcinoma.

Juvenile myxedema or cretinism has been present in ten per cent of cases of lingual thyroids, suggesting a hypofunction of the gland in this location. Small lingual thyroids, however, have been found in normal, euthyroid people. There have been no reported cases of hyperthyroidism associated with isolated lingual thyroids. In those few cases in which hyperthyroidism has been described, cervical thyroids have been assessed clinically to be present. About eleven cases of carcinoma have been reported.<sup>14</sup> All cases have occurred in males and most have been over thirty-five years of age.

### Treatment

In the majority of asymptomatic cases, it is not necessary to biopsy a mass at the base of the tongue which demonstrates thyroid function by  $I^{131}$  uptake. There have been reports of postbiopsy infection, slough, and inflammatory reaction which have made subsequent resection unsatisfactory.<sup>15</sup> Lingual thyroids in males over thirty-five years of age should be at least biopsied if not excised, because carcinoma has occurred in this group.

Small asymptomatic lingual thyroids do not require active treatment, and periodic examination will suffice. Parents of young girls may be advised that the mass may become symptomatic during puberty or pregnancy. Large symptomatic masses causing dysphagia, dyspnea, dysphonia, ulceration, or hemorrhage require therapy. If pretracheal thyroid is also present, surgical excision of the lingual mass will cure the patient. If, as in seventy per cent of cases however, the lingual thyroid constitutes all of the patient's functioning thyroid tissue, therapy is not so simple. While complete surgical excision is the best treatment in these cases, lifelong post-

operative thyroid replacement is unavoidable. Attempts at subtotal excision have not prevented myxedema in a majority of cases and regrowth with return of symptoms has occurred in thirteen per cent of cases.<sup>16</sup> The oral route for excision is adequate for most cases, but the transhyoid and lateral pharyngotomy approaches have been used for large lesions.<sup>17</sup> Tracheotomy is occasionally necessary for the immediate postoperative period. Use of  $I^{131}$  has made exploration of the pretracheal region for thyroid tissue unnecessary in most instances.

Prevention of postoperative myxedema by an autograft transplant of the lingual thyroid is a logical goal. Autografting into the rectus abdominis muscle has been tried in a number of cases with only partial success. Successful grafts have been reported which have not fully supplied the thyroid needs of the individual.<sup>18,19</sup> Transplanted thyroid tissue in children has had a limited capacity to regenerate and grow, necessitating thyroid extract supplementation to supply increased metabolic needs. A few cases have been reported of submucous dissection of a lingual thyroid from surrounding tissues followed by successful transposition of the gland with a large muscle pedicle flap into the submental space.<sup>20</sup>

$I^{131}$  ablation of the lingual thyroid has been the chief competitor to surgical therapy. The main argument for  $I^{131}$  therapy is that the treatment is non-surgical, is taken orally in a few doses, and facilitates any subsequent surgery by decreasing vascularity of the gland. In contrast to surgery, however,  $I^{131}$  therapy causes a slow regression of the mass which is often incomplete with persistence of symptoms. Regression is often a matter of several months or years.<sup>21,22,23,24</sup> As with surgery,  $I^{131}$  therapy necessitates lifelong thyroid replacement therapy.  $I^{131}$  in therapeutic doses has been restricted in children because of its possible deleterious effects.

In all cases of lingual thyroid, one should look for evidence of hypothyroidism, with retarded development, dry pasty skin, lethargy, cold intolerance, increased weight, or thinning of the eyebrows. A Protein Bound Iodine determination and a serum cholesterol along with the  $I^{131}$  uptake will help to evaluate total thyroid function.

Many of the simple hypertrophies of lingual thyroid tissue may be a response to a functional thyroid insufficiency. Treatment with thyroid extract and iodine if necessary would in theory be beneficial in these cases. There have been satisfactory reports with this physiological medical management. In most instances, however, the duration of treatment has been less than six months and longterm followups are lacking. Perhaps those cases which are mildly symptomatic could be given

a full six months trial of thyroid extract to obviate the need for surgery.

### Summary

Caution should be exercised in the excision of cyst-like masses at the base of the tongue, because such removal may deprive the patient of his only functioning thyroid tissue. The embryology, diagnosis, pathology, and treatment of lingual thyroids is discussed.

### Acknowledgment

The  $I^{131}$  scintigram was done by the Radioisotope Department of Richard P. Spencer, M.D.

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But the peculiar evil of silencing the expression of an opinion is, that it is robbing the human race; posterity as well as the existing generation; those who dissent from the opinion, still more than those who hold it. If the opinion is right, they are deprived of the opportunity of exchanging error for truth: if wrong, they lose, what is almost as great a benefit, the clearer perception and livelier impression of truth, produced by its collision with error..

—John Stuart Mill



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ORVAN W. HESS, M.D.

*President*

## THE PRESIDENT'S PAGE

I am grateful for the honor bestowed on me by election to the office of President of the Connecticut State Medical Society in this 174th year of its existence. I assume the responsibility with a sense of humility and I sincerely appreciate the opportunity to serve the members of the Society in this capacity.

Changes in patterns of providing medical services are considered by many to be an integral part of the movement which has been active on many socioeconomic fronts during the past decade. Improved transportation and communication facilities, shifting densities of population and increasing specialization by doctors are other factors which have played a significant role in modifying the traditional methods of providing health care for the people and furthering the trend toward concentration in medical centers. Technological progress in instrumentation and the use of sophisticated accoutrements for the diagnosis and treatment of disease have further necessitated the establishment of focal points for these purposes in hospitals and institutions. While offering certain advantages for patients requiring this special level of care, the number that can be accommodated is limited. The acute need remains for more extensive clinical application to the day-to-day medical requirements of the population at large in both urban and rural areas. Closer integration and coordination of services to fit the circumstances is indicated.

Among the many expressed objectives of the public health agencies, the desire to improve the delivery of health services to all, community by community, has the support of most physicians. The methods proposed to accomplish this aim and the portent of federal involvement have not met with similar approval. The long struggle between the Government and Medicine over "medicare" legislation is documentary evidence.

1966 will mark the inception of a new relationship between Government and the Profession in the provision of health care for the Aged. Since Congress passed the Medicare Law (P.L. 89-97) nearly a year ago there have been numerous discussions, explanations and assessments of the content and implications of the Law. Yet, on the eve of its implementation, many questions of doctors and the administrators of hospitals and other facilities, remain unanswered. The extent of the burden which may be placed on hospitals by demands of those having entitlements under provisions of the Law is unknown. Although many hospitals in Connecticut have large numbers of patients already waiting for admission, we are assured by some that there will probably be no acute scarcity of beds. Of great concern, however, is the problem of the manpower needed to fully implement the program. Shortages in many categories seem almost inevitable. Some depletion in the pool of available physicians will result from commitments to active duty with the Armed Forces and others may not elect to participate in Medicare programs. Adequate augmentation of nurses and technicians does not seem likely in the near future. Unless these problems are met and overcome, it appears that Medicare will make it difficult to preserve present standards of high quality service to the entire population.

ORVAN W. HESS, M.D.



# FROM THE GENERAL MANAGER'S OFFICE

WILLIAM R. RICHARDS, M.D., *General Manager*

160 St. Ronan Street, New Haven, Conn.

Telephone 865 0587

Josephine P. Lindquist

*Assistant to General Manager*

## SUMMARY OF ACTIONS COUNCIL MEETING

**Wednesday, March 23, 1966**

### **I. Attendance**

Present in addition to the Chairman, Dr. S. J. Martin, were: Drs. Cullen, Hess, Bradley, W. Martin, Weise, Sr., M. Caplan, Brandon, H. Caplan, Pitock, Rogol, Grendon, Egan, Deming, Spitz, Palumbo, Shepard, Ayres, Ciccarella, Cramer, Fabro, Abbot, Petrie, Wilson and Roch. Also present were: Mrs. Lindquist, Mr. Chilcoat (AMA), and Dr. Richards. Absent were: Drs. Goldberg, Gardner, Nolan, Epstein (resigned) and Hastings.

Joining the Council as invited guests were: Commissioner Bernard Shapiro and Medical Director Edwin R. Connors, State Department of Welfare; Commissioner Franklin M. Foote, State Department of Health.

### **II. Routine Business**

#### **Approval of Minutes**

It was VOTED to approve the minutes of the meeting of February 17, 1966, as printed and distributed, with the addition of the item under which Max Caplan, Meriden, reported on this participation in the Planning Committee for the 1967 (State Health Department) seminar on hospital infections, the report having been accepted as information.

#### **Life Memberships**

It was VOTED to approve applications for Life Membership received from the following eligible Active Members of the Society:

- John C. Carrozzella, Wallingford (NHCMA)
- Richard J. Hinchey, Waterbury (NHCMA)
- James H. Inkster, Fitzwilliam, N.H. (FCMA)
- Max H. Ruby, Middlebury (NHCMA)
- Gaetano R. Sandulli, Waterbury (NHCMA)

#### **CSMS Membership Dues Exemption**

It was VOTED to exempt from payment of CSMS 1966 membership dues (renewable) the following Active Member:

Gerald N. Cimmino, Derby (NHCMA)—Military Service.

#### **Appointment of Representative—Mental Health Conference**

It was VOTED to designate James C. Johnson, Jr., Hartford, as CSMS representative to the 12th

Annual Conference of State Mental Health Representatives, Chicago, March 18-19, and to request Dr. Johnson to file a report with the Council on the proceedings of the Conference. A member of the CSMS Committee on Mental Health, Dr. Johnson will be reimbursed for usual expenses in attending the meeting by AMA.

#### **Resignation—Representative to Connecticut Health League**

It was VOTED to accept, with regret the resignation of Morris A. Granoff, New Haven, as a Representative to the CHL (1964-67); to elect D. Norman Markley, Hartford, as a Representative to the CHL to complete Dr. Granoff's unexpired term; and to designate John J. Scanlon, Norwalk as Chairman of the 3 Representatives for 1966-67.

#### **Vacancy—1966 Conference Committee for the Improvement of the Care of the Patient**

It was VOTED to accept, with deep regret, notice that D. Dillon Reidy, Hartford (a long-time member of this Committee and present Chairman thereof) had died on March 8, 1966. Action to replace Dr. Reidy on the slate of nominees for 1966-67 was tabled.

#### **Information re Nomination to Hospital Planning Commission**

It was VOTED to accept, as information, notice from Mr. A. M. Rogers, President of the Connecticut Hospital Planning Commission, that he believes "it will be possible to consider adding Dr. David A. Grendon, Sharon, (a CSMS nominee) as a Director at the Annual Meeting which is tentatively scheduled for December of 1966". Dr. Grendon was nominated by the Council to replace Gaert S. Gudernatch, Sharon, who was unable to accept service with the Planning Commission.

#### **Date of Next Council Meeting**

The date for the next meeting of the Council was set for Thursday, April 21, 1966.

### **III. Old, New and Special Business**

#### **Report of Representative—AMA 62nd Annual Congress on Medical Education**

It was VOTED to accept, with special commendation, a report filed by Charles B. Cheney, New Haven, on the proceeding of this 62nd Annual Congress, and to submit the report to the Editor

of the Journal for publication in *CONNECTICUT MEDICINE*. Dr. Cheney is a member of the CSMS Committee on Medical Education and Licensure and of the Connecticut Medical Examining Board, and attended the Congress as a representative of the Society.

#### **Reports—The Committee on Hospitals**

It was VOTED to accept, as information, two reports filed by the Committee on Hospitals as follows:

(a) Memorandum on meetings with Health Commissioner Franklin M. Foote re certification of institutional providers of health services under Part A of Medicare, with special reference to the function of "utilization review committees" in sampling and reviewing patients' charts, and the matter of immunity from civil suit of physicians serving on such committees. In essence, the Committee has advised the Commissioner to set minimum standards (at least at the outset) for the former, and to investigate the legal considerations of the latter.

(b) A memorandum summarizing the progress that has been made thus far to implement the provisions of P.L. 89-239 (Heart Disease, Cancer, Stroke and Related Diseases) in Connecticut. In essence, the Committee reports that the UConn and Yale Medical Schools are applying to USPHS for "planning funds", with a view to making the State a single "region" for a medical program and to have the two Medical Schools designated as the "centers" for such program. The Committee concurs with the Council's previously-taken position that medical practitioners should be given substantial representation on the "regional advisory board" (to the medical program) which P.L. 89-239 calls for.

#### **P.L. 89-97—Proposed Policies for Certifying Home Health Agencies**

Commissioner Franklin M. Foote, State Health Department, joined the Council to present the policies he proposes to use to certify "home health agencies" as providers of services under Part A of Medicare and to answer questions concerning same. In brief, the Commissioner proposes to use the same criteria in this regard that his Department has used in the past for "Evaluating the Administration of a Public Health Nursing Service" with respect to servicing communities of limited populations, and to follow the policy that: "In each community or area a single home health agency will be approved, with preference given to that agency which provides the most comprehensive family-centered skilled nursing and other therapeutic service." This limitation to a single agency will not, of course, preclude the approved agency from subcontracting with other agencies in that community or area to furnish services which the single agency does not provide

(speech therapy, physiotherapy, etc.). Having heard the Commissioner's presentation, the Council VOTED to approve, in principle, his proposed policies for the certification of home health agencies under Part A of P.L. 89-97.

#### **Resolution—CSMS Section on Anesthesia**

It was VOTED to accept, as information, notice that the Section on Anesthesia has adopted a resolution on the subject of separate billing by hospital-based specialists, identical with similar resolutions previously adopted by the Sections on Pathology, Radiology, and Physical Medicine. On December 9, 1966, the House of Delegates endorsed the principle of such separate billing by *all* hospital-based specialists, and the Council has taken steps to enlist support for this principle among other medical organizations, hospital staffs, third party payment agencies, and the State Commissioners of Insurance and Workmen's Compensation.

#### **CSMS Policies re Reimbursement of Physicians by Government Agencies**

At the Council meeting of February 17, 1966, acting on a report of the Committee on Third Party Payments re "suggested conversion factors" to be offered to governmental third party payment agencies for use with the CSMS Relative Value Schedule, the Council voted actions as follows:

"(a) To accept the report, with commendation, but to recommend that the suggested conversion factors *not* be used to set up payment schedules at this time.

"(b) To commit the Council to the concept of 'usual and customary fees', as determined at local level, and to recommend that the Relative Value Schedule and other available means be used by all concerned (advisory committees to governmental third parties) to implement this concept."

At this meeting, the Council received two communications concerning these February 17 actions. The first was a resolution from the New Haven County Medical Association's Board of Governors, expressing the opinion that the subject actions were contrary to a directive of the House of Delegates (April 27, 1965) that "suggested conversion factors" be offered to such governmental agencies and, for that reason, urging "the Council to reconsider" these actions and "to approve the suggested conversion factors" submitted by the Committee on Third Party Payments for use by the Society's advisory committees (to the Welfare Department, Dependents Medical Care, etc.)

The second communication was from the Chairman of the Committee on Third Party Payments, requesting (for the Committee) that the Council define terms embodied in its February 17 actions



as follows: "usual and customary fees", "determined at local level", and "other available means".

In response to the NHCMA Board of Governors' resolution, without actually voting to "reconsider", the Council VOTED to reaffirm, without change, the two actions on the report of the Committee on Third Party Payments which it had taken on February 17 (See (a) and (b) above).

In response to the request for definition of terms, filed by the Committee on Third Party Payments, the Council VOTED to approve a document (prepared by the staff) tentatively titled: "Restatement of CSMS Policies on Reimbursement for Physicians' Services, with Particular Reference to Governmental Third Party Payment Agencies", and to transmit same to the House of Delegates on April 26, 1966, with a recommendation that it be adopted by the House. A suitably edited copy of the document is attached to these minutes for members of the Council and will be published as a "Report of the Council" in the Delegates Handbook for the Annual Meeting of the House of Delegates in April.

Further, it was VOTED to inform all members of the Society promptly, using a suitable communications medium, of the Council's position on "usual and customary fees, as determined at local level" as the basis for reimbursing physicians for their services, and the reason for the Council's decision of February 17 *not* to offer suggested *statewide* conversion factors to governmental third party payment agencies for use with the CSMS Relative Value Schedule (as authorized by the House of Delegates' action, April 27, 1965) at the present time.

**Proposed Connecticut Implementation of Title XIX of P.L. 89-97**

Commissioner Bernard Shapiro and Medical Director Edwin R. Connors, of the State Welfare Department, joined the Council to present and discuss the Commissioner's plans to implement Title XIX of P.L. 89-97 in Connecticut, effective July 1, 1966. Having previously submitted printed copies of the proposal to all Council members, the Commissioner enlarged upon various aspects of his plans and answered questions pertaining thereto.

Following Mr. Shapiro's presentation, it was VOTED to approve, in principle, his plan for implementing Title XIX for categorically indigent and medically indigent residents of Connecticut who are 65 years of age and older, such plan to become effective on July 1, 1966. In brief, the plan would place the over-65 group eligible for tax-supported medical assistance under the Federal "Medicare" program, utilizing Parts A and B up to the limits of the coverage provided, and supplementing Parts A and B, when necessary, with Kerr-Mills funds (un-

covered services, deductibles, co-insurance, etc.). Pursuant to this plan, it should be noted that the Connecticut General Life Insurance Company, the "carrier" for Part B, intends to reimburse physicians on the basis of usual and customary fees, and that Commissioner Shapiro has agreed to let Connecticut General act as fiscal agent for his Department in all aspects of Part B, *including* the payment of deductible and co-insurance obligations of the over-65 beneficiaries enrolled under Part B.

It was further VOTED *not* to approve of the balance of the Welfare Department's proposed plan for implementing Title XIX to cover eligible Connecticut residents *under* age 65, and to inform the Commissioner that the Council cannot approve this portion of the plan unless physicians are to be reimbursed for their services on a "usual and customary fee" basis under this portion, as is to be done by Connecticut General under Part B of Title XVIII of P.L. 89-97. The Council was pleased to note, however, the Commissioner's declared intent to support the principle of "usual and customary" reimbursement of physicians under this portion of Title XIX, with the understanding that he or the Society or both will introduce a bill concerning said principle at the next session of the General Assembly.

**Report—CSMS Committee on Relative Value Study**

Stewart P. Seigle, Chairman, filed a report of the Committee on Relative Value Study concerning its findings to date on its review of the "experience of the Society and its members" with the Relative Value Schedule adopted by the House of Delegates on April 27, 1965. In brief, the report states that while it may be assumed that a substantial number of members are aware of the existence of an official CSMS Relative Value Schedule, it is doubtful that more than a few are actually "using" it for any constructive purposes. The request of the Committee on Third Party Payments for "suggested conversion factors" from the various CSMS Sections and related groups (a listing of which is included in the report), and the "fee survey" currently being conducted unilaterally by Connecticut Medical Service, Inc., have apparently stimulated a considerable wave of interest in the Relative Value Schedule among physicians in the State—many of whom are apparently examining the document for the first time since it was mailed out to all members of the Society last July. In addition, the Committee reports that it is seeking and receiving suggested changes in the Schedule (unit values, nomenclature, etc.) from the CSMS Sections and other groups which participated in the original RV Study (1959-64), and that the Committee's recommendations concerning

such changes will be the subject of an additional report to be filed (hopefully) in time to present to the House of Delegates on April 26, 1966.

It was VOTED to accept the RVS Committee's report and recommendations, and to transmit the substance of the report to the House of Delegates at the forthcoming Annual Meeting. The "recommendations" dealt with the need for more education of physicians regarding relative values and their uses, and the desirability of having a continuing and active Committee on Relative Value Study. It was further VOTED to request the Chairman of the Committee, Dr. Seigle, to select a subcommittee from the membership of the present committee, and at large, to study and report to the Council on suitable mechanisms for carrying out an educational program on relative values for the membership.

**Report—Delegate to the Medical Society of State of New York**

Ralph L. Gilman, Storrs, filed a report on his attendance at the Annual Meeting of the Medical Society of the State of New York as a delegate from CSMS. Since James R. Cullen, President, was unable to attend, Dr. Gilman also served as Dr. Cullen's official representative at the meeting. It was VOTED to accept this report as information, and with thanks.

**Progress Report—Council Committee on Preliminary Study of Censorship Questions**

J. Alfred Fabro, Chairman of this Committee, filed a progress report of the Committee concerning its study of proper procedures to be followed by the Society in hearing appeals on matters of discipline affecting members, particularly with reference to appeals taken on decisions of the component county medical associations, and other pertinent matters on the subject of medical ethics and discipline which are, or should be, within the jurisdiction of the State Society. It was VOTED to approve the report, in principle, and to direct the Committee to proceed to implement the mechanisms for CSMS disciplinary procedures outlined in, and recommended by, the report, and to make a subsequent report on these matters to the Council.

**Report—Committee on Public Health**

Having been informed by the Committee on Public Health that the first "regional" or "district" health department has been formed jointly by the Towns of Westport and Weston, it was VOTED to urge county association public health committees to promote the establishment of similar "combined" district health departments among appropriate smaller communities in their areas of jurisdiction.

**Interpretation of CSMS Bylaws re "Suspension"**

A problem was noted that the HCMA has "suspended (a physician) from membership", which deprives the physician of all rights and privileges of membership including "the duty to pay dues", and that the CSMS bylaws (as amended 12/9/64) state that, ipso facto, such a physician shall become a "member under suspension (but still a CSMS member)", losing the rights to vote and hold office, but "shall be required to pay membership dues to the Society". To resolve this relatively minor disparity between the HCMA and CSMS bylaws, it was VOTED, that, upon payment of CSMS membership dues, the named physician be carried as a CSMS "member under suspension" (in accordance with the CSMS bylaws), and that on his membership card and in the Roster that he is under suspension and will so remain until restored to membership in good standing by the Hartford County Medical Association.

N.B.: *The foregoing is a summary of the proceedings and actions of the Council on March 23, 1966. Detailed minutes of the meeting are on file at 160 St. Ronan Street, New Haven, for perusal by any interested member of the Society.*

## 1966 MEETINGS

**May 19-26**—Symposium on Psychiatry and Neurology: A Practical Approach, to be held at Mound Park Hospital Foundation, Inc., 701 Sixth Street, South, St. Petersburg, Florida 33701. For further information address: Neurology, Mound Park Hospital Foundation, Inc., St. Petersburg, Florida 33701.

**May 25**—"Gaylord Day" to be held at Gaylord Hospital and Sanatorium, Wallingford, Connecticut from 2:00 P.M. to 6:00 P.M.

**June 7**—The New Haven Branch American Cancer Society will hold their 22nd Annual Dinner Meeting at 7:00 P.M. in the New Haven Lawn Club.

**September 28**—41st Connecticut Clinical Congress to be held at Mary S. Harkness Auditorium, Yale University Medical School, New Haven, Connecticut. The program will be devoted to "Recent Advances in the Diagnosis and Management of Liver Disease" and "Recent Advances in the Diagnosis and Management of Thrombophlebitis."



## PLACEMENT WANTED

**OBS-GYN** — Military and Board requirements completed, subspecialty training in gynecological cancer. Seeks opportunity for solo, partnership or association within traveling distance of New York City beginning July, 1966.

**PEDIATRICIAN**—39 years of age, presently completing military obligations. Would like to associate with another pediatrician within traveling distance of New York. Available July 1, 1966.

**GENERAL SURGEON**—35 years of age, Board eligible, Connecticut license. Military obligations completed. Would like to join a group or form an association. Available as of July, 1966.

**GENERAL SURGEON**—34 years of age, Board eligible, Connecticut license. Military obligations completed, would like to associate with another surgeon or become part of a group practice. Available July 1, 1966.

**UROLOGIST** — Board eligible, Connecticut license. 34 years of age, with military obligations completed. Available July, 1966 and would like to enter into an association or a solo practice.

**UROLOGIST**—31 years of age, military obligations completed. Board eligible, Connecticut license. Would like to enter group practice as for July 1, 1966.

**G.P.**—39 years of age, military obligations completed. Would like to practice with either a group or an associate as of June, 1966 when he will return to this country from England.

**INTERNIST**—34 years of age, Board eligible. Would like to form either an association or enter into group practice either in Hartford or New Haven areas. Available shortly, upon fulfillment of exchange visitor's status from Canada.

**DERMATOLOGIST**—Board eligible, military obligations completed. Would like either group or associate practice. Available as of July, 1966.

**OBS-GYN**—Connecticut license, Board eligible, military obligations completed. Wishes to practice with a group or an associate. Available within one month's notice, 42 years of age, married.

**GEN. SURGEON**—33 years of age, Board certified and also Board eligible in Thoracic Surgery, wishes to practice with an associate. Connecticut license, military obligations completed.

**INTERNIST** or **G.P.** for three-man group. Have regularly visiting specialist consultant staff, modern clinic facilities, scheduled training and vacation periods. Starting net income \$15,000 to \$18,000 depending on qualifications. Partnership in one year.

**WANTED** — Locum tenens in September for general practitioner with view to permanent association to follow.

**DIRECTOR OF PREVENTABLE DISEASES**—Health Department, New Haven, Conn. Responsibility includes supervision of tuberculosis, venereal disease and epidemiological programs. Opportunity to develop new chronic disease programs and conduct research in a University City undergoing extensive physical and social redevelopment. Eligibility for Conn. Medical license required; training or experience in public health desired. Apply to John B. Atwater, M.D., Dr. PH, Director of Health, 161 Church St., New Haven, Conn. 06510.

**ANYONE INTERESTED IN THE ABOVE IS ASKED TO CONTACT THE GENERAL MANAGER'S OFFICE, 160 ST. RONAN STREET, NEW HAVEN, CONN. 06511**

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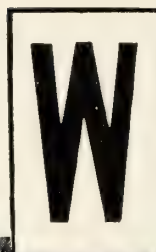
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## SPECIAL REPORT

### Legal Opinion Regarding The Supervision Of Psychologists By Psychiatrists

*The following is a summary of an opinion by legal counsel of Wiggin and Dana, requested by the Committee on Mental Health of the Connecticut State Medical Society. It was requested in connection with a particular occurrence which raised questions concerning the professional liability of legitimate concern to psychiatrists as well as to the wide variety of professions with whom psychiatrists characteristically work. That the opinion centers on relations between psychologists and psychiatrists reflects only the fact that the occurrence in question concerned these two professions. The legal opinion, itself, is quite clearly broader in scope and essentially sets forth considerations of a general type.*

#### Introduction

Many of us are aware of the growing effectiveness of communication between psychiatrists and psychologists in this State. In recent years we have been developing a firm, frank, and productive relationship and we would not want this legal opinion in any way to affect adversely this development. With this interest in mind, a meeting was held to consider how best to bring this information to the attention of all parties concerned. Representatives of the Connecticut Psychological Association, the Connecticut District Branch of the American Psychiatric Association, and the Committee on Mental Health of the Connecticut State Medical Society gathered to consider this problem in an atmosphere of cordiality and frank discussion. Attention was focused on how best to disseminate this material and not on policy statements of who is privileged to do what professionally according to whom. Discussion yielded the consensus that the legal opinion be circulated with these few prefatory paragraphs.

It will be seen that the opinion concerns the liability of the psychiatrist *when he is in a supervisory role or when he is clearly and actively affecting diagnosis and treatment*. The opinion is not relevant where any other type of relationship exists or where the different professions are engaging independently in their traditional roles. It may be of interest to the reader to know that there is no instance to date, known to us, of any psychiatrist in the State of Connecticut being charged or held liable for the activities of psychologists with whom he has associated himself.

\* \* \* \* \*

#### The Question

The Committee on Mental Health authorized by the Council of the State Medical Society submitted to Counsel of the Connecticut State Medical Society the following question:

Many patients suffering from psychiatric disorders seek treatment either in outpatient clinics or in the

offices of psychiatrists in private practice. In many clinics a psychiatrist is in charge and a psychologist will undertake certain forms of treatment, essentially psychotherapy, under the supervision of the psychiatrist. In this situation, the psychologist is technically an agent of the psychiatrist and where supervision of the psychologist, is in fact, provided, the patient is well-protected.

Because of particular situations, especially where there is a lack of psychiatrists, some patients attend a clinic, are seen only by a psychologist or social worker, and are treated by a psychologist without a psychiatrist ever seeing the patient and sometimes without the psychiatrist, in fact, discussing the patient with the psychologist in a supervisory role. Moreover, certain situations have developed where special clinics have been set up, such as for student health at universities and other schools of higher learning, where a psychiatrist is technically in attendance but also never sees or discusses the patients with the psychologist who is actually treating individuals attending for therapy.

Another variety of this situation is where a psychologist in private practice theoretically is treating a patient under the supervision of a psychiatrist but, again, there is little, if any, contact between the psychologist and the psychiatrist.

The opinion sought, therefore, is what legal responsibility and what legal peril does a psychiatrist involve himself in when he knowingly participates in such arrangements, that is, when he cooperates professionally with a psychologist who is treating a patient whom he, the psychiatrist, has never seen but whose treatment he is supposedly supervising?

This problem will, undoubtedly, become even more widespread in the future if various plans on a Federal and State level are developed and many psychiatrists are asking the above questions.

Counsel for the State Medical Society gave a lengthy opinion of which the following is a summary:

## The Summary

(1) A psychiatrist may be personally liable for the malpractice or other improper professional acts of a psychologist who is treating a private patient if

(a) an agency relationship does in fact exist, as where the psychiatrist supervises, controls or employs the psychologist, or

(b) the psychiatrist participates in or actively assumes responsibility for diagnosis or treatment by the psychologist.

This possible liability exists whether or not the psychiatrist has any personal contact with the patient.

(2) A psychiatrist who is employed by any clinic or hospital and who is, by the nature of his responsibilities in the clinic, supervising the treatment of a patient administered by a psychologist might well be held liable or responsible for claimed malpractice or other improper acts on the part of the psychologist. It is the opinion of Counsel that upon the facts stated the clinic or hospital as the ultimate employer might also be held liable (subject to the rules of charitable immunity) and as a practical matter it would probably be the more likely target of any claim of malpractice.

(3) If a physician refers a patient to a psychologist for treatment and if the patient is led by the physician to believe that the psychologist is functioning as an agent of the physician, the latter exposes himself to the possibility of personal liability for claimed malpractice and perhaps other improper acts on the part of the psychologist.

It is the opinion of Counsel that where a patient is referred to a psychologist (who is not, as distinct from a psychiatrist, a licensed doctor of medicine) no assurance can be given that the referring physician could not be held liable for alleged malpractice of the psychologist even where the latter is not found to be the agent of or otherwise under the control of the referring physician.

John A. Atchley, M.D. (1957-1965)

E. Lloyd Dawe, M.D.

Jean G. deChabert-Ostland, M.D. (1957-1965)

Frederick J. Flynn, M.D.

James C. Johnson, Jr., M.D.

Walter W. Kemp, M.D.

Richard T. Kramer, M.D.

William Lee, M.D.

John E. Morrison, M.D.

John Donnelly, M.D., Chairman

Committee on Mental Health

Connecticut State Medical Society

## PLACEMENT OPPORTUNITIES

**CLINICAL DIRECTOR**—To develop program in psychiatric hospital with emphasis on psychosomatic medicine. Opportunity for experience in employees' health clinic, workmen's compensation, clinic and psychopharmacologic drug research. Will direct department already staffed by seven doctors. EEG, EKG, Ophthalmology and Radiology Depts. already fully equipped and staffed. Consultants available in every medical and psychiatric specialty. Opportunity for program to be affiliated with Yale, Wesleyan, UConn and local general hospitals. All particulars should be sent in first letter, including references. Apply; John F. Lowney, Jr., M.D., Supt., Connecticut Valley Hospital, Box 351, Middletown, Conn.

**WANTED, COLLEGE PHYSICIAN** — For women's college, 1400 students. Out-patient and in-patient services, with nursing staff and laboratory. Full or part-time. Write: Mary N. Hall, M.D., Connecticut College, New London, Connecticut.

**INTERNIST**—Board certified or eligible Internist wanted to take over fully established practice and office or physician who is leaving Conn. shortly. Located in Glastonbury, Connecticut, just a few minutes from Hartford Hospital.

**PATHOLOGIST**—500 bed general, medical and surgical hospital for male Connecticut resident veterans. Salary range \$14,740 to \$19,000. Excellent fringe benefits, including group life insurance, Major Medical Insurance and Social Security. Housing accommodations available at low-cost maintenance. For further information, contact: Personnel Office, Veterans Home and Hospital, Rocky Hill, Connecticut.

**DISTRICT HEALTH DIRECTOR** for Weston/Westport, Conn. Requires M.D. plus degree in Public Health or equivalent experience. Salary range \$18,500 to \$22,500, to be negotiated, depending on qualifications. Start: July, 1966. Send resume to: Clifford Mills, M.D., Chairman; Weston-Westport Health District; c/o Dept. of Health; Westport, Conn. 06880.

**OBS-GYN associate.** Board eligible or certified. Essential that physician speak French and military duties completed. To assume full practice on retirement in two or three years. Located in a large, expanding central Connecticut city.

**PEDIATRICIAN**—Third Pediatrician to join two other physicians presently practicing in Waterbury, Connecticut. Hospital facilities located nearby in growing, industrial city.



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FORMULA— Alcohol . . . . . 70%  
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By providing more comfort and extra sleep for the baby, DENTOCAIN LOTION MILD grants the mother greater peace of mind and several additional hours of necessary rest.

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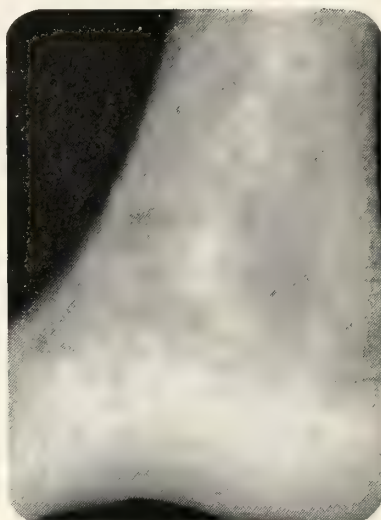


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# eczema: scourge of childhood



R. R., Age 11—Before treatment—  
atopic eczema of long standing



After treatment—with ARISTOCORT  
Topical Ointment 0.1% for two weeks

ARISTOCORT® Triamcinolone Acetonide Topicals have proved exceptionally effective in the control of various forms of childhood eczema: allergic, atopic, nummular, psoriatic, and mycotic.

In most cases responsive to topical ARISTOCORT, the 0.1% concentration is sufficiently potent. The 0.5% concentration provides enhanced topical activity for patients requiring additional potency for proper relief.

*Administration and Dosage:* Apply sparingly to the affected area 3 or 4 times daily. Some cases of psoriasis may be more effectively treated if the 0.1% Cream or Ointment is applied under an occlusive dressing.

*Contraindications:* Tuberculosis of the skin, herpes simplex, chicken pox and vaccinia.

*Precautions and Side Effects:* Do not use in the eyes or in the ear (if drum is perforated). A few individuals react unfavorably under certain conditions. If side effects are encountered, the drug should be discontinued and appropriate

measures taken. Use on infected areas should be attended with caution and observation, bearing in mind the potential for spreading of infection and the advisability of discontinuing therapy and/or initiating antibacterial measures. Generally, dermatological conditions may require systemic corticosteroid therapy. Steroid therapy, although responsible for remissions of dermatoses, especially of allergic origin cannot be expected to prevent recurrence. The use over extensive body areas, with or without occlusive nonpermeable dressings, may result in systemic absorption. Appropriate precautions should be taken. When occlusive nonpermeable dressings are used, miliaria, folliculitis and pyoderma will sometimes develop. Localized atrophy and striae have been reported with the use of steroids by the occlusive technique. When occlusive nonpermeable dressings are used, the physician should be aware of the hazards of suffocation and flammability. The safety of use on pregnant patients has not been firmly established. Thus, do not use in large amounts or for long periods of time on pregnant patients.

*Packages:* Tubes of 5 Gm. and 15 Gm.; ½ lb. jar.

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## SUMMARY OF PROCEEDINGS

### HOUSE OF DELEGATES — ANNUAL MEETING

#### Hartford, Connecticut — April 26, 1966

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#### Reports And Addresses

The House received a number of reports and/or addresses from the officers of the Society, its Divisional Boards and Committees, and several distinguished guests. Those reports and addresses submitted in printed form will be published in this and succeeding issues of the *Journal*. The "Supplementary Report of the Council," presented by Dr. Stevens J. Martin, Chairman, and the address of the President of the Woman's Auxiliary to CSMS, Mrs. William R. Richards, appear at the end of this summary of proceedings.

#### Election Of Officers, Committees, Advisors And Representatives

The officers elected at this meeting of the House were:

President: Orvan W. Hess, New Haven

President-Elect: E. Tremain Bradley, Norwalk

Vice-President: Norman H. Gardner, East Hampton

Secretary: Waldo E. Martin, Milford

Treasurer: Isadore S. Goldberg, Torrington

Speaker of the House: Kenneth F. Brandon, Hartford

Vice-Speaker of the House: Henry Caplan, Yalesville

AMA Delegates (January 1, 1967 to December 31, 1968): J. Alfred Fabro, Torrington; Max Caplan, Meriden

Alternate AMA Delegates (same terms) Ellwood C. Weise, Sr., Bridgeport; Morris P. Pitock, Bridgeport

Councilor-at-Large: Charles Polivy, Hartford

A full slate of Boards, Committees, Advisors, Representatives, etc. was also elected by the House. Each member of these groups will be formally notified of his or her election, and the membership of all Boards, Committees, etc. will be published in the (August) 1967 Roster.

#### Delegates From Other Medical Organizations

Introduced to the House and making brief remarks were:

J. Dunbar Shields, M.D.: Delegate from the New Hampshire Medical Society

William M. Stahl, M.D.: Delegate from the Vermont Medical Society

Robert W. Buck, M.D.: Delegate from the Massachusetts Medical Society

Henry I. Fineberg, M.D.: Delegate from the Medical Society of New York

Lloyd A. Hamilton, M.D.: Delegate from the Medical Society of New Jersey

Robert M. Knowles: Delegate from the Maine Medical Association

Armand Archambault, M.D.: President, Council of New England State Medical Societies

John W. Patterson, M.D.: Dean, University of Connecticut Medical School

#### Presentations And Awards

##### 1966 CSMS Press Awards

Luca E. H. Celentano, Chairman of the Public Relations Division, informed the House that due to circumstances beyond the Division's control, it was not possible to judge the entries submitted for 1965-66 in time to make a report to this meeting.

##### AMA Awards Of "Certificates of Humanitarian Service"

Bearing the inscription: "In recognition of meritorious service performed for the medical profession, the United States Government and the people of South Viet Nam by treating the ill and injured during his voluntary medical mission in South Viet Nam," plaques awarded by the American Medical Association were presented by President Orvan W. Hess to three Connecticut physicians.

The recipients were:

Haakon Ragde, M.D., Waterbury

J. Alfred Fabro, M.D., Torrington

Arnulf vanDyke, M.D., New London

##### AMA-ERF Grants For 1966

Presented by retiring President James R. Cullen, AMA-ERF checks were received by the Yale School of Medicine and the University of Connecticut School of Medicine. The major grant (\$6,529) went to the Yale School, but a "token" gift (\$53) also went to the UConn School, which, being still in the planning stage, is not yet eligible to share in the distribution of unrestricted AMA-ERF funds.

Accepting these grants were:

Arthur Ebbert, Jr., M.D., Associate Dean, Yale School of Medicine

John W. Patterson, M.D., Dean, UConn School of Medicine

#### **Presentation Of Past President's Pin**

In appreciation for his many contributions to the Society and its members, James R. Cullen, Hartford, received a Past President's Pin as he retired from office (1965-66). Making the presentation was Stevens J. Martin, Hartford, Chairman of the Council.

#### **Presentation: Pictures On History Of Medicine**

Accepting on behalf of the Society, President Orvan W. Hess received four framed reproductions of original paintings on the History of Medicine which were presented to the Society by Parke, Davis and Company. Making the presentation for Parke, Davis were: Mr. W. E. McCormick, N. E. Regional Manager, and Mr. Ray Johnson, Field Manager. The pictures will be hung in the Society's headquarters building in New Haven.

#### **Educational Grant To COMPAC**

Upon recommendation of the Council, it was voted to authorize the Treasurer to disburse \$5,000 of the Society's reserve funds to the Connecticut Medical Political Action Committee as a grant in support of political education activities of that organization. This marks the third year in which the House has authorized such a grant, contributing \$3,000 to COMPAC in 1964 and \$5,000 in 1965.

#### **Honorary Memberships And M.D. Degrees**

At the request of the Litchfield County Medical Association, and upon recommendation of the Council, the House voted to elect three distinguished doctors of medicine to Honorary Membership in the Society and to bestow Honorary M.D. Degrees on two prominent lay persons. These honors were granted under the provisions of Article VII, Section 1, Paragraphs 5 and 6 of the Bylaws, and certificates will be presented to the recipients at the June ceremonies to be held by the Litchfield Association in conjunction with its Bicentennial Celebration.

The background and credentials of those so honored by the House follow:

##### **Honorary Membership**

DR. HOWARD R. CRAIG, born in 1894, received his M.D. degree from Cornell in 1919, practiced pediatrics in New York City from which he retired to take on the position of Executive Director of the New York Academy of Medicine. He is a summer resident of Sharon, has a strong feeling for medical

and Litchfield County history, is well-known and loved in this community for his medical and historical work, and is an unofficial member of our Bicentennial Committee to which he has given much help and advice.

DR. F. PEYTON ROUS, born in 1879, who obtained his A.B. and M.D. degrees from Johns Hopkins, the latter in 1905, and is a resident of Cornwall. He is world-renowned for his work in physiology and pathology, and is a Nobel prize winner for his discoveries on the interrelationships between viruses and cancer. He is an Emeritus member of the Rockefeller Institute of Medicine, was co-editor of the Journal of Experimental Medicine, a member of many national and international societies of physiology and medicine including being a past president of the Harvey Society, and a fellow of the New York Academy of Medicine.

DR. BYRON P. STOOKEY, of New York City, and formerly of Sharon, who was born in 1887 and received his M.D. degree from Harvard in 1913. He is the former Professor of Neurosurgery at Columbia College of Physicians and Surgeons, and used to be on the staff of Sharon Hospital. He is a member of many national and international surgical and neurological societies, the describer of numerous neurosurgical syndromes and techniques, and an astute investigator and discoverer of historical material which led directly to the accurate dating of the founding of the Litchfield County Medical Society, and its establishment as the oldest county society in the country.

##### **Honorary M.D. Degree**

MARK VAN DOREN, Ph.D., of Cornwall, a beloved educator and author, who has broadened the scope of intellect and range of enjoyment of countless thousands of individuals with whom he has come in contact over many years. He is the son of a country doctor and his sympathies have been with that profession for many years.

JOHN B. BLAKE, Ph.D., a young native of Connecticut, who graduated from Yale before serving in the Air Force in World War II, and then obtaining his M.A. and Ph.D. degrees from Harvard in the fields of public health and history of medicine. He is a historian at the Rockefeller Institute for Medical Research in New York City and is now Executive Secretary of the American Association of the History of Medicine and a curator of the Division of Medical Sciences of the Smithsonian Institute in Washington. He grew up in an environment of medicine in New Haven where his father was a professor at Yale Medical School. He is well schooled in the history of medicine in New England and is the first speaker on our Bicentennial Program on the subject of colonial medicine.



## **Resolution On Discrimination In Organized Medicine**

As recommended by the Council, it was voted to adopt for transmittal to the June meeting of the AMA House of Delegates a resolution as follows:

SUBJECT: DISCRIMINATION IN ORGANIZED MEDICINE

WHEREAS: Since 1939, resolutions have been presented to the House of Delegates of the American Medical Association stating that "membership in constituent state associations and component county or district societies shall not be denied on the basis of race, creed or color," therefore be it

RESOLVED: That the House of Delegates of the Connecticut State Medical Society go on record as approving fully the principle that membership in the American Medical Association of any constituent association shall be revoked if such constituent association shall allow any of its component societies to deny membership to any individual on the basis of race, creed or color, and be it further

RESOLVED: That the Society's Delegates to the American Medical Association introduce the foregoing resolution at the June, 1966 meeting of the AMA House of Delegates and work to secure its adoption by that body.

## **Statements Of CSMS Policy On Reimbursement For Physicians' Services**

As prepared and submitted by the Council, it was voted to adopt the following report:

SUBJECT: RESTATEMENT OF CSMS POLICIES ON REIMBURSEMENT FOR PHYSICIANS' SERVICES, WITH PARTICULAR REFERENCE TO GOVERNMENTAL THIRD PARTY PAYMENT AGENCIES

(1) It is the policy of the Connecticut State Medical Society that, in *all* patient-physician relationships, each licensed practitioner of medicine is privileged to determine for himself the usual fee that he will charge for each professional service he renders; that, however, he has the responsibility to set his usual fees at levels within the range which is *customary to the community or regional area of his practice* for similar services; that he has the further responsibility to explain the nature and amount of his charges to his patients and to any other party legitimately concerned with his rendering of, or billing for, services; and that when his fee is questioned by his patient or other legitimately concerned party as to its propriety with respect to *usual and customary* standards for his area of practice, such question may be referred for review and recommendation to an authorized committee of the physician's local or county medical society having jurisdiction in that area. (Based on: "Certain Policies of the CSMS re Inter-Relationships Between the Patient, the Physician, and Third

Party Entities," adopted by the CSMS House of Delegates, April 30, 1963.)

(2) It is the policy of the Connecticut State Medical Society that whenever government (federal, state or local) assumes responsibility for the payment of medical care charges, whether by a governmental agency directly or through an intermediary, the same principles of "usual and customary" reimbursement stated in Paragraph (1) shall apply; i.e., the principle of reduced or substandard payments shall *not* apply. (Based on "Report of the Committee on Third Party Payments—Revisions of Welfare Payment Schedules," approved by the CSMS House of Delegates, April 27, 1965).

(3) It is the policy of the Connecticut State Medical Society that all agencies offering insurance-type coverage which proposes to help persons pay for physicians' services, in full or in part, shall be authorized and encouraged to use the official CSMS Relative Value Schedule, as adopted in 1965 and as may be amended from time to time, as a guide to bringing into and maintaining in proper relationships the various services performed by doctors of medicine that are included in the coverage offered by such agencies (Based on recommendations embodied in "The Report of the Relative Value Study Committee," adopted by the CSMS House of Delegates, April 27, 1965.)

(4) It is the policy of the Connecticut State Medical Society to recognize that the monetary levels of usual and customary fees vary somewhat throughout the State, particularly with respect to what is considered to be *customary* in the many different community and regional areas. Hence, the Society recognizes that governmental agencies accepting the Society's stated principles on usual and customary fees as the basis for reimbursing physicians may need guidelines to assist them in calculating realistically the amounts of the appropriations that must be sought from legislative and administrative bodies to fund insurance-type medical care programs paying claims on that basis. In the light of these considerations, and for the express and sole purpose of assisting such agencies to make such realistic calculations, the Society will offer suggested conversion factors (subject to periodic review and adjustment) to be used in conjunction with the CSMS Relative Value Schedule *only*.

Such conversion factors have already been derived from suggestions made by CSMS Sections and other professional groups representing almost all types of medical practice on a *statewide* basis. Used as "guides" in the manner stipulated above, and in conjunction with other pertinent actuarial determinants (expected frequency of claims, utilization of services, etc.), the dollar values to be sug-

gested will be comprehensive enough to enable governmental third parties to calculate realistically the funds (appropriations) that will be needed to accommodate most recognized variations of usual and customary charges in the State, as determined *at local or regional level*. Their being offered to qualifying governmental agencies for this purpose, and for this purpose *only*, is in no way to be interpreted by anyone as authorizing their use to establish fee schedules, since such usage would be entirely contrary to the Society's long-standing policy that "it (the Society) refrain from making statements, endorsements, agreements and the like which would, or might appear to, commit any of its members to accepting involuntarily a fixed schedule (of payments) for their professional services." This policy is applicable whether any such "fixed schedule" should be set at either higher *or* lower levels than fees usual and customary to any given community or regional area in the State. (Based on: "Certain Policies of the CSMS re Inter-Relationships Between the Patient, the Physician, and Third Party Entities", adopted by the CSMS House of Delegates, April 30, 1963).

(5) It is the policy of the Connecticut State Medical Society that all component county medical associations and, if necessary, all local or regional medical societies, should have committees-in-being which are authorized to receive, review, and make recommendations on all questions relating to usual and customary fees in their areas of jurisdiction, and that such committees should make their review functions readily available to all governmental agencies (or their fiscal intermediaries) which have accepted the Society's stated principles on usual and customary fees, determined at local level, as the basis for reimbursing physicians for medical care rendered to their beneficiaries. (Based on the principles enunciated in the "Report of the Ad Hoc (Bradley) Committee on Resolution No. 2", approved by the CSMS House of Delegates, April 27, 1965).

The adoption of these five statements of CSMS policy by the House of Delegates means that all CSMS committees which are advisory to governmental third party agencies are authorized and directed to assist such agencies "to develop schedules (of reimbursement) that conform with the principle of parity of payments to physicians in the State, in line with 'usual and customary' charges" by advancing the policies as follows:

a. Seeking acceptance by such agencies of the Society's principles on usual and customary fees as the basis for reimbursing physicians for their services.

b. Seeking, conversely, to eliminate the current policies of such agencies which offer physicians "re-

duced or substandard" reimbursement for their services.

c. Encouraging the use of the CSMS Relative Value Schedule by such agencies to bring into and maintain in proper relationships the various services performed by doctors of medicine that are included in the coverage provided.

d. Offering suggested dollar conversion factors, in conjunction with the CSMS Relative Value Schedule (as outlined in Paragraph (4) above), for the purpose stipulated, and for that purpose *only*.

e. Offering the "review committee" mechanism (as outlined in Paragraph (5) above) as a sound and workable method of protecting the proper interests of all concerned with respect to claims made against the agencies' funds on the basis of usual and customary reimbursement of physicians for their services.

Pursuant to the adoption of this report, related actions were taken as follows:

IT IS MOVED: That the House of Delegates instruct the Council to make available to all CSMS advisory committees to governmental third party payment agencies appropriate RV unit conversion factors, as recommended by the CSMS Committee on Third Party Payments, and to authorize such advisory committees to use such factors as guidelines, in conjunction with the CSMS Relative Value Schedule, to implement fully the objectives of the "statements of policy" on physician reimbursement adopted by the House of Delegates at this meeting; and it is further

MOVED: That the previous policy of the Society (adopted on April 26, 1965) concerning usage of conversion factors in conjunction with the CSMS Relative Value Schedule when negotiating *payment schedules* with governmental third parties is herewith rescinded.

#### **Resolution On Medical Assistance Programs Under Title XIX Of P.L. 89-97**

Having heard the report of the Council on the Welfare Department's plans for implementing Title XIX of P.L. 89-97 in Connecticut, effective July 1, 1966, it was voted to adopt a resolution (with minor editorial change) as follows:

BE IT RESOLVED: That if Welfare Commissioner Shapiro will, in his Department's 1967 budget, incorporate funds sufficient to cover the expense of paying doctors of medicine on the basis of their usual and customary fees under Title XIX of P.L. 89-97, the Connecticut State Medical Society will support such a budget and do all things possible to obtain its approval by the General Assembly, and be it further

RESOLVED: That it be reiterated to Commissioner Shapiro that, under no circumstances, will the Con-



necticut State Medical Society approve any policy of his Department for reimbursing doctors of medicine that involves the principle of reduced or sub-standard payments for physicians' services.

It was further voted to inform Commissioner Bernard Shapiro, State Welfare Department, of this action.

### **Proposal To Amend The CSMS Charter**

Pursuant to a proposal to make past presidents of the Society *voting* members of the House of Delegates, the Council reported that it is the opinion of legal counsel that to effect such a change in the Bylaws would require that an amendment to the Charter be sought as a Special Act of the General Assembly; further, that to seek such a Special Act in the absence of one or more pressing reasons would be undesirable (see Item VI of "Report of the Council", which follows this summary of proceedings). Accepting the recommendation of the Council, it was voted *not* to approve the proposal to make past presidents of the Society voting members of the House of Delegates, and, hence, not to seek an amendment to the Charter from the General Assembly.

### **Progress Report—Experience With CSMS Relative Value Schedule**

A progress report on this subject was accepted as part of the "Report of the Council". A summary of the findings and conclusions of the experience review now being made by the Committee on Relative Value Study appears under Item XIII of the Council's report.

### **SUPPLEMENTARY REPORT OF THE COUNCIL**

MR. SPEAKER, MR. PRESIDENT, MEMBERS OF THE  
HOUSE AND DISTINGUISHED GUESTS:

At the last meeting of the House of Delegates in December of 1965, a motion introduced from the floor—and subsequently adopted—suggested that the natives are prone to grow just a little bit restless when the reports emanating from the Speaker's rostrum are either very numerous or very lengthy or both. While the aforesaid motion actually applied only to our *semi-annual sessions*, I trust you will note that those who address you today—including the Chairman of the Council—are making a sincere effort to be brief and to the point, while, at the same time, not leaving things unsaid which should rightfully be brought to your attention. I might say parenthetically, however, that most of Medicine's current concerns—and there are more in the immediate offing—do not lend themselves readily to superficial examination, thumb-nail condensation and twenty-five words or less solutions.

Your Council has met ten times during the year, and it was my privilege to summarize the first six of these sessions for you on December 9th last. The published "Report of the Council" which appears in your Handbook (at the top of Page 17) is short, and it is so intentionally. As Chairman, I have placed the onus on each of you to re-read or read for the first time—as the case may be—the detailed minutes of the January, February and March Council meetings which have been mailed to all listed members of the House from the Society's headquarters in New Haven. It is the Council's sincere wish to share its deliberations with the Delegates while they are still timely, and this policy of widely distributing the minutes has been in effect for more than three years.

Bacon once said "Reading maketh a *full* man," and, further, that "a conference maketh a *ready* man." Accordingly, I am confident that you are *full* from your reading of these minutes and have come to this conference *ready* to wisely transact our business today. Bacon also said that "writing maketh an *exact* man," and I have therefore put into writing for presentation now only those matters of continuing interest which I believe will contribute to the *exactness* of your understanding of the Council's stewardship in the first quarter of 1966, up to and including its most recent meeting on April 21st. If there are questions on matters not covered in this limited, oral report, I shall be pleased to try to answer them.

### **I. COMMITTEE ON MEDICAL QUACKERY**

In January, the Council took steps to initiate the formation of a Committee on Medical Quackery, under the chairmanship of Dr. Max Caplan of Meriden. As you know, quackery in its various forms costs the American public dearly in money and in lives, year after year, and it is felt to be important to have a committee-in-being to study and report continuously on matters relating to this subject of national concern. Dr. Caplan, you may recall, played a key role in planning and staging a Connecticut Congress on Medical Quackery several years ago—an event which received favorable acclaim from both public and professional sources.

### **II. HEALTH EDUCATION AND THE VENEREAL DISEASE PROBLEM**

Dr. Hyman A. Levin, New Haven, filed an excellent and comprehensive report with the Council on his attendance at the recently-held AMA National Symposium on Venereal Disease as a representative of the Society. Dr. Levin's report was turned over to our Committee on Public Health "for study and recommendation, in concert with the Commissioner of Health, with a view toward committing the Society to the support of the efforts of Dr. Foote and others to make health and sex education a more meaningful, regular part of the curricula of our public schools and state-supported colleges and

universities." Those who take cognizance of the alarming increases being reported in the incidence of venereal disease, especially among teenagers, know that a monumental task faces us all in trying to regain the effective control over gonorrhea and syphilis that was achieved in the decade or so following the end of World War II.

### III. THE COMMITTEE ON HOSPITALS

The Committee on Hospitals, under the able and progressive chairmanship of Dr. Leopold M. Trifari of Hamden, has had one of its most productive years and has been of invaluable assistance to the Council on matters relating to the Medicare Law, the DeBaKey legislation, and other important subjects. The report of this Committee is published in your Handbook, beginning on Page 18, and I understand that its chairman will present to us today a supplementary report on activities engaged in as recently as a week ago. At its last meeting, the Council considered one of the supplementary matters which Dr. Trifari will cover. This concerns a recommendation of the Committee on Hospitals that the Council form a new Ad Hoc Committee on Medicare Experience (for want of a better name). I shall leave it to Dr. Trifari to give you the details of the proposal, but, in essence, such an Ad Hoc group would receive, evaluate, correlate and report on problems encountered by physicians in rendering services to patients under Title XVIII and Title XIX of Public Law 89-97. The Council has heartily approved this recommendation, and will fully implement it as soon as possible after you have elected the related committees for the coming year.

I feel sure the House will share the Council's disappointment that Dr. Trifari will find it impossible to carry on as chairman of the Committee in 1966-67, and will join the Council in commending him for a job well done during his many years of service in that capacity.

### IV. PUBLIC LAW 89-239—THE SO-CALLED "DEBAKEY LEGISLATION"

As most of you know by now, the Yale and UConn Schools of Medicine have applied to the Federal authorities to be designated as the "centers" around which a "regional medical program" for Connecticut is proposed to be established. If the application is approved, study grants will be forthcoming from Washington, D. C. in the near future, with additional and substantial implementing funds to be made available when the study has been completed. The Council has urged that full representation on the Advisory Council to the program be given to medical practitioners, and commends the appointment of Dr. Orvan W. Hess, our incoming president, as an excellent step—but only a first step—in that desired direction.

The enactment of P.L. 89-239 by the Congress was prompted, in large part, by allegations that such legislation constituted an absolute necessity

if the public health was to be adequately protected. For this reason, it is hoped that a wry smile here and there may be forgiven by our political saviors when it is revealed that one of the first—and major—objectives of the preliminary study to be carried out is to determine to what extent such a regional medical program is *really* needed in our State. It is probably safe to predict, however, that the before-placed *cart* of our needs will be found to be of sufficient size to justify the subsequent acquisition of what promises to be an extremely expensive horse to *push* it—expensive in its appetite not only for tax dollars but also for medical resources and manpower which are, even now, in somewhat short supply.

### V. PROPOSED INCREASE IN AMA MEMBERSHIP DUES

At its interim meeting in Philadelphia last Fall, the AMA House of Delegates gave tentative approval to an increase in AMA membership dues from \$45 a year to \$70 a year, commencing January 1, 1967. At the forthcoming June meeting, it is expected that the Delegates will be asked to confirm that action.

For those of you who do your homework regularly—at least those who are AMA members, you will by now have perused carefully the detailed explanation of the organization's current and projected financial situation which was presented in the February 21st issue of AMA NEWS, a publication that is mailed to you each week. For those who have not seen this fact sheet, perhaps Dr. Norman Gardner or another of our AMA Delegates would be willing to offer a thumb-nail sketch of the major considerations which form the basis for the proposal.

Normally, we do not instruct our Delegates, either pro or con, preferring to leave it to their own good judgment to support, oppose, or appropriately modify motions and resolutions coming before the AMA House. The Council recommends that we follow this policy in the present instance, but feels that it might be helpful to our representatives to be given a little informal grassroots opinion on the dues question. We suggest, therefore, that the Speaker ask for a show of hands as a sampling of your opinion.

This House is, of course, privileged to make its own ground rules on handling informal matters of this kind, but it would seem to me that only AMA dues-payers would wish to participate in such a more or less off-the-record expression of opinion. After all, Gimbel doesn't tell Macy, nor do members of one of our county associations cast ballots on business of primary concern to members of the others.

### VI. PROPOSED AMENDMENTS TO THE BYLAWS

On March 23rd, the Council received from its Subcommittee to Study and Revise the Bylaws a comprehensive report, with recommendations, on a number of matters referred to the Subcommittee



during the past 18 months. On Pages 49, 50 and 51 of your Handbook, the proposed amendments approved by the Council are published in some detail—indicating in each instance what the amendment is intended to accomplish and providing the specifics of the necessary changes to be made. *The Council recommends* the adoption of these amendments, with one exception to which I will refer in a moment, and places them on the table for final consideration and action at our 1966 semi-annual meeting.

The exception is listed under No. I of the series; i.e., the proposal to make past presidents of the Society voting members of the House of Delegates. You will note that it is the opinion of our legal counsel that (a) this proposal will require an amendment to our Charter; that (b), such an amendment would have to be sought as a Special Act of the General Assembly; and that (c), it would hardly seem worthwhile to seek a Special Act from the Assembly for this single purpose.

On page 49 of the Handbook, it is stated that the Council requests the House to “vote its opinion concerning this proposal” as to our past presidents. However, at its meeting on April 21, having reviewed the appraisal rendered by our attorneys, the Council voted to *recommend specifically* that the proposal be *disapproved* by this body. In today’s political climate, it is felt by some that to expose our Charter to the tender mercies of the legislature—in the absence of pressing reasons for so doing—might turn out to be a Pandora’s box-type venture, as a result of which we could get more amendments made to our precious parchment than we bargained for; some, perhaps, that we would just as soon do without.

**VII. 1966 EDUCATIONAL GRANT TO COMPAC**

On April 21, the Council voted to recommend to the House of Delegates that authorization be given to our Treasurer to disburse the sum of \$5000 of our general funds as a grant to the Connecticut Medical Political Action Committee to support the political *educational* activities of that organization. As you know, this House voted in 1961 to encourage the formation of a political action committee in Connecticut which would be administered entirely separately from the Society, and, in 1962, COMPAC was formed independently by a group of members of the Society. Two years ago, our legal counsel gave us clearance to make such educational grants—I stress the word “*educational*,” and, at the direction of the House in each case, the Council awarded \$3000 to COMPAC in 1964 and another \$5000 last May.

**VIII. HONORARY DEGREES AND MEMBERSHIPS**

In conjunction with the Bicentennial Celebration of the Litchfield County Medical Association, and in compliance with the request of that Association, the Council is pleased to commend to the

House of Delegates, for approval, the following nominations:

**For HONORARY MEMBERSHIPS:**

- Dr. Howard R. Craig, New York City (Sharon)
- Dr. F. Peyton Rous, Cornwall
- Dr. Byron P. Stookey, New York City (formerly of Sharon)

**For HONORARY M.D. DEGREES:**

- Mark Van Doren, Ph.D., Cornwall
- John B. Blake, Ph.D., Washington, D. C. (born in Connecticut)

The authorization for the House to bestow these honors is provided for in our Bylaws, Article VII, Section 1, Paragraphs 5 and 6. If approved, it is planned to ask our incoming president, Dr. Hess, to present suitable certificates of award to the recipients at the Litchfield Bicentennial Celebration ceremonies in June.

**IX. RESOLUTION ON DISCRIMINATION IN ORGANIZED MEDICINE**

Published on Page 47 of your Handbook is a resolution on discrimination in organized medicine, which the Council adopted on February 17, and *recommends* that you approve by an action today. We have since been notified that the Board of Directors of the Hartford Association subsequently adopted a practically identical resolution at a meeting of that body on March 23rd.

Here in Connecticut, of course, discrimination on the basis of race, creed or color does not exist in medicine—either in our medical organizations, in our hospitals or in any other facets of our professional lives. We have good reason to believe that great progress has been made throughout the nation in drying up this limited—but still chronic—source of injustice to qualified practitioners of medicine. Whether the resolution before you today, or some different mechanism, proves to be *the* way to dispel this bothersome cloud, once and for all, the Council believes that no doctor anywhere should be content to rest until the desired goal has been achieved completely.

**X. PROGRESS REPORT—DECEMBER 9TH NEW HAVEN COUNTY RESOLUTION**

At the last meeting of the House, a resolution introduced by the New Haven County delegation was adopted and the Council was directed to report to *this* meeting on the progress which has been made toward implementing its *resolves*. In essence, the purpose of the resolution is for the Council to study certain deficiencies in the coverage of physicians’ services which presently exist in several of our State’s tax-supported medical care programs and to seek ways by which such coverage can be made more comprehensive. While much of the Council’s time is currently being spent on matters closely related to this subject, I can only inform you today that the specific resolution in question is still under study by Dr. Ente’s Committee on Third

Party Payments; that progress is being made in accordance with the directive of the House; and that we may anticipate receiving a definitive report on it in the foreseeable future.

#### **XI. CHANGE OF PERSONNEL IN OUR PUBLIC RELATIONS DEPARTMENT**

At its February meeting, the Council was notified by Mr. James G. Burch—who has been our Director of Public Relations for nearly two decades—that “for personal reasons” he found it necessary to resign from that position, effective April 1, 1966. Many of you knew Jim—as most of us called him—to be a loyal employee who made innumerable friends in, and *for*, the Society. Having accepted Mr. Burch’s resignation, with regret, the Council sought and has been successful in obtaining a well qualified replacement for him on our headquarters staff. It is my pleasure to announce to you that Mr. Peter F. Villano, of New Haven, has accepted the post of Director of Public Relations and Communications for the Society, and, while he will not be joining us fulltime until June 1st, I hope that as many of you as possible will have an early opportunity to make his acquaintance—and he *yours*.

#### **XII REPORT OF THE NOMINATING COMMITTEE**

As you know, the Council is the *Nominating Committee* of the Society. Starting on Page 39 of your Handbook, the Council-approved slate of nominees is published. Under *officers*, it is my duty to inform you that Dr. Stewart P. Seigle, Hartford, asked that his name be withdrawn as nominee for the post of Delegate to the AMA (one of two which you are to elect today) and, hence, at its April 21 meeting, the Council voted to make changes as follows

For AMA Delegate—J. Alfred Fabro, Torrington

For Alternate AMA Delegate—Ellwood C. Weise, Sr., Bridgeport

The Max Caplan-Morris P. Pitcock nominations for the other posts of AMA Delegate and Alternate remain unchanged.

#### **XIII PROGRESS REPORT—REVIEW OF EXPERIENCE WITH THE RELATIVE VALUE SCHEDULE**

Pursuant to the adoption of an official Relative Value Schedule at our last annual meeting, a directive was issued that: “After a trial period of approximately twelve months (the Council was to) review and evaluate the experience of the Society, its committees, its members, and the component county associations in using the Relative Value Schedule” and report to the House on the findings. Accordingly, at the Council’s request, a reactivated Committee on Relative Value Study, under the chairmanship of Dr. Stewart P. Seigle of Hartford, began this review and evaluation several months ago and filed its initial report on March 23rd. The pertinent conclusions reached thus far can be summarized as follows:

(1) It is fair to say that the adoption of an official Relative Value Schedule by the House of Delegates about a year ago has probably had little or no real influence on the individual fee patterns of physicians practicing in Connecticut. It appears that, except for some of our state and county socio-economic committees and the executive boards of some of our Sections, few doctors have made more than a casual attempt to accommodate their own fee structures to the listing of relative value units. For this reason, the Council has recommended that a *subcommittee* of the full RVS Committee be selected by Dr. Seigle to plan and implement an educational program on the relative value concept for the members of the Society. This single technical aid cannot be expected to solve every problem that faces us, but, unless its principles are well-understood by a broad segment of the membership, it will be most difficult to lay a firm foundation for our current and future socio-economic policies.

(2) Dollar conversion factors for possible application to our Relative Value Schedule have been sought from, and suggested by, the executive committees of most of the Sections and other groups that participated in our original Relative Value Study. However, Dr. Seigle’s Committee is of the opinion that the dollar values submitted represent the collective thinking of the respective executive committees, but are not and might not necessarily be subscribed to by the membership at large. This does not mean at all that the factors suggested are considered to be inappropriate. It means only that the direct application of conversion factors to the Schedule could be a practice fraught with appreciable danger, *unless and until* most practitioners fully understand not only the relative value concept itself but also the short and long range significance of setting up *any statewide fee schedule* by such application.

Another important facet of the Committee’s review is still being pursued and will be reported on subsequently. This concerns the potentially complex task of obtaining recommended changes in the Schedule proper (i.e., the changing of unit values for certain listed services; modifications in the length of required after-care; alterations of the nomenclature and the addition of unlisted services; and so on). When all desired changes have been filed by the participating Sections and groups, the Committee will correlate them, assess their propriety, and submit to the House for official approval such changes as will improve the Schedule *without* violating the principle of relative value.

#### **XIV. COMPREHENSIVE REPORT ON THE MEDICARE LAW AND TITLE XIX OF P.L. 89-97**

I have now reached the last item in the Council’s report, and I warn you in advance that it will be a



somewhat lengthy one. Within only a matter of weeks from now—on July 1st—our Federal and State governments propose to implement—almost *in toto*—what has been aptly called the “most far-reaching piece of social legislation ever enacted in the history of the world.” Title XVIII of the Social Security Amendments of 1965 guarantees so-called medicare benefits for the elderly—some twenty millions of them, and Title XIX provides similar tax-supported health benefits for a veritable host of totally indigent, semi-indigent, and categorically-related indigent persons of all ages. It has been predicted that, when operating full swing, these two programs may ultimately involve *some 50 per cent or more of the total population of the United States*. We can only hope that the other half of the citizenry—the group into which most physicians fall—will be able to provide the means to finance these admittedly costly undertakings.

In November, the Council had prepared and distributed as a supplement to the Journal an “assessment of the professional implications” of P.L. 89-97, as they were understood to apply at that time. It was—and remains—the Council’s intention to prepare and distribute further informational materials to our members on Medicare and Title IX when the rules and regulations being drafted by the authorities become known. I regret to report that, although literally a dozen or more rule books the size of urban telephone directories have already been issued by the Social Security Administration, it remains a fact that questions that appear simple and basic to us still cannot be answered—not even by highly-placed officials in the Social Security Administration itself.

In baseball parlance, it is often said that you can’t hit what you can’t see, and I suspect that this time-honored axiom will also apply to Medicare and the rest of these programs—at least at the outset. In the opinion of experts far more knowledgeable than we are, the initial impact of these complex laws will fall on a public, a hospital system, and a medical profession which are, for the most part, totally unprepared to absorb it. Elderly patients will be in the dark as to their entitlements, institutional providers of service will be distraught with the rules they must follow and the host of forms they must fill out, and physicians—well, as usual, they will be trying to figure out how to continue to practice good medicine in spite of the hot breath of bureaucracy impinging on their collective necks.

I now propose to tell you what the Council knows—or thinks it knows—about various aspects of Titles XVIII and XIX:

#### **(1) Medicare “A”**

We have had excellent liaison with Commissioner Franklin Foote concerning the certification of in-

stitutional providers of service by the Health Department. Working closely with our Committee on Hospitals, and with the Council, Dr. Foote has again demonstrated his sincere desire to move cooperatively with the Society on matters of concern to medical practitioners. This is not the time to go into the specifics of the rules and regulations applying to hospitals, nursing homes and home health agencies under Part A—many of the specifics are not yet known—but it is recommended that the medical staffs of hospitals and doctors connected with other types of institutional care providers work diligently and continuously with the administrators of such agencies to assure that local interpretations conform with local professional standards.

#### **(2) Medicare “B”**

As most of you know, the administration of Medicare B—which will help the elderly pay their doctors’ bills—has been assigned to the Connecticut General Life Insurance Company. Representatives of the Company have been very forthright with Council representatives—and with many of the county and local medical associations—in outlining the policies under which they hope to operate the plan. In brief, they propose to pay 80 per cent of “usual and customary fees”, *as determined at local level* (providing the patient has satisfied the \$50 per year deductible), with the patient being responsible to the physician to pay the 20 per cent of co-insurance. The usual and customary aspects of a given fee of a given physician practicing in a given locality will be measured against Connecticut General’s considerable experience with this concept, and, in questionable cases, it is planned to seek the advice of the applicable medical organization to counsel the Company as to what its maximum liability should be—not as to the ethical propriety of the charge.

The physician will be given one option to bill his patients directly (i.e., *not* submitting a claim form). Then, upon presentation of the physician’s *receipted* bill, the patient will be reimbursed by the Company in the prescribed amount. The other option allowed will be for the physician to accept assignment of benefits from the patient, in which case, upon submission of a properly completed claim form, the Company will pay 80 per cent of the fee to the physician directly, with the patient again being responsible to take care of the 20 per cent co-insurance segment.

The Council has been impressed by Connecticut General’s outline of what the Company proposes to do and urges all members of the Society, individually and in groups, to cooperate with the carrier to the fullest extent possible. However, since the

road to hell is often paved with good intentions, the Council urges everyone to keep in mind that, in this instance, the Company is, *in fact*, an agent of the Federal government and, therefore, subject to rules and regulations imposed from above. Such regulations must necessarily be passed along to both beneficiaries *and* physicians, and hence we must remain on the alert to help the Company help itself whenever the Federal heat is becoming oppressive.

### (3) Title XIX

Commissioner Bernard Shapiro of the Welfare Department has presented to the Council and its Committees his plans for implementing Title XIX in Connecticut. Again, in the interests of time, I will not review the details of these. Suffice it so say, that as to the part for covering the elderly (OAA and MAA cases) the Council has voted to approve this plan, in principle. Since Connecticut General will administer the entire program for physicians' services, it will not differ substantially from Medicare B, except, of course, that it would be absurd to bill indigent patients directly.

As to the second portion of the plan—which will cover all other categories of wards of the State, the Council has informed the Commissioner that the Council cannot approve any policy of reimbursing physicians which does not adhere to the Society's usual and customary fee concept. Mr. Shapiro appears willing to go along with this concept, in principle, but apparently feels he cannot finance a program embracing it fully until sufficient funds are appropriated by the next General Assembly.

### (4) The Report Of The Council On Physician Reimbursement Policies

Since it is evident that, as time goes on, more and more people will have their doctors bill paid, all or in part, by governmental third party agencies, either directly or through an intermediary, the Council considers to be of the utmost importance to effectively advance the principle of INDIVIDUAL RESPONSIBILITY, as defined by this House in 1963, and, in particular, the concept of USUAL AND CUSTOMARY FEES, AS DETERMINED AT LOCAL LEVEL, as the proper and equitable basis for *all* third party reimbursement of physicians for their services.

Governmental agencies, without exception, look to the Society as the official representative of the medical profession in Connecticut, and we must have policies to guide us and them which are both constructive and workable. Starting at the bottom of Page 47 of your Handbook, the Council presents such a policy document for your approval today. I believe the report is largely self-explanatory and

needs no further comment until you are prepared to act upon it.

On recommendation of the Committee on Third Party Payments, the Council is prepared to submit for your approval, if desired, the *suggested conversion factors* alluded to at the bottom of Page 48, in the left-hand column.

In conclusion, I take this opportunity to thank the officers and other members of the Council for their wholehearted cooperation and sage advice in these critical times. Also to our General Manager, Mrs. Jo Lindquist and the other dedicated people on the Society's staff, I publicly express my gratitude.

Respectfully submitted,

STEVENS J. MARTIN, M.D.  
*Chairman*

### ADDRESS OF THE PRESIDENT OF THE CSMS WOMAN'S AUXILIARY

MR. SPEAKER, MR. PRESIDENT, MEMBERS OF THE HOUSE OF DELEGATES AND DISTINGUISHED GUESTS:

It is indeed an honor for the president of the Woman's Auxiliary to address the House of Delegates of our parent organization, the Connecticut State Medical Society. I welcome this opportunity to tell you briefly about some of the Auxiliary's activities this past year and, perhaps, even bring to your attention one or two of its problems.

Prior to 1965, it was customary to hold our Board meetings at various country clubs and restaurants throughout the State, and, as a consequence, we had the feeling that we were without any real *home*; that we had no headquarters to give us a sense of permanency and administrative continuity. Hence, this year the Board sought to find a centrally-located regular meeting place, and I am pleased to report that one was found. With the kind cooperation of the staff at St. Ronan Street, we arranged to hold our sessions at the Society's New Haven office building and to keep our records there for ready reference. The arrangement has worked out very well, and, in addition, has furnished us with several valuable fringe benefits. The geographical convenience has increased the number of participants in our meetings. The quiet atmosphere of the Barker-Weld Room has been conducive to an orderly transaction of our business. Availability to our files and other sources of first-hand information has enabled us to function more efficiently. And, finally, we have had a chance to try to establish better rapport between our Board members and members of your Council. Last May, following the annual meetings of the two organizations, the Board prepared an informal buffet luncheon as a "get-acquainted"



gesture toward the Council and the Society's staff—an event which turned out to be both well attended and well received. My successor as president of the Auxiliary, Mrs. John D. O'Connell of Hartford, is planning to repeat the luncheon this year, and it is my hope that, in the future, it may be continued as an annual affair.

A concerted attempt has been made in the past twelve months to develop better liaison between all Auxiliary members at all levels. We recognize that each of us have what we might call *provincial* interests in our local and county areas, but we feel that it is of the utmost importance to have unity of understanding, purpose and action among us in matters of statewide and national concern. In this endeavor, the Woman's Auxiliary to the American Medical Association has been of great assistance. In addition to improving substantially its published communications—such as DIRECT LINE, a newsletter for leaders which is mailed four times a year to state chairmen and county presidents, and M.D.'s *Wife* (formerly *The Bulletin*), which is received bi-monthly by all members of the Auxiliary—our national federation also held a series of Regional Workshops in the early fall of 1965 to which were invited state presidents and state committee chairmen on AMA-ERF, Community Service, Membership, Legislation, Mental Health and Health Careers.

At state level, our Board sought to spread the word on the programs recommended by national by inviting our county presidents-elect and committee chairmen to come to our September and October meetings to discuss plans with those from Connecticut who had attended the Workshop for our area which was held in New York City. Being realistic, I feel sure that not *every one* of these recommended projects was carried out fully in *every* county or *exactly* as suggested, but it is the hope of the Board that the opportunity to *know* about them has stimulated an interest to do something with at least *some* of them at grass roots level.

Our State Society Advisors — in particular Dr. Orvan Hess, and your General Manager—who just happens also to be my husband, have been most generous with their time and energies in keeping our Board informed on the essentials of the Medicare Law, the doctor-draft and other important matters, many of which I see are on your agenda today. I wish, too, to make special mention of the help and frequent courtesies extended to us by Mrs. Jo Lindquist and her capable assistants. It is true that the Auxiliary serves secondary functions of a social and administrative nature, but our primary purpose is to support our husbands—the Connecticut medical profession—in their efforts to keep their chosen calling unregimented and, thereby, to assure

that their patients will continue to receive the high quality of care that mutual freedom to choose has made possible. To this end we are dedicated, but to this end we can make no meaningful contribution unless we are acting in concert with you—unless you take us into your confidence, *fully* and *frequently*.

I said earlier that we have a problem or two—and we do. The area of difficulty I wish to mention today is one that I am told we face jointly with you—the problem of limited and inequitably shared participation in our work. *Auxiliary membership* in Connecticut currently stands at 1,146. Since the *Society's* membership now numbers just over 3,600, this means that less than one doctor's wife in three is putting a shoulder to our common wheel; that less than one in three are giving so much as a few dollars a year in dues to help us discharge our responsibilities. This anemia of involvement is prevalent to a greater or lesser degree all across the country, and in some states—through the medium of composite billing to physicians—husband-wife *team* enrollment has produced up to 100 per cent auxiliary membership. Here and there, I have noted some enthusiasm for this approach to be taken in our State—but opinion on this is somewhat divided among doctors' wives, and, I suspect, might be even more divided among doctors themselves. Our organizations have traditionally drawn their strength and support from voluntary sources, and we all abhor the thought of compulsion. However, while we in the Auxiliary will continue to enroll new members, one by one and on an individual basis, we hope that the Society's leadership will give a little extra thought to this bothersome problem of ours and advise us as to what new paths we might take to try to resolve it.

As president of our State Auxiliary, I have been honored to spend the past year in service to causes in which I personally believe. I have done my best to advance the objectives of the Auxiliary which, as you know, are also the objectives of the Society. In so doing, I have enlarged my circle of valued acquaintances and added to my understanding of medicine and the people who practice it. Once again, I thank all of you here at this meeting of the House of Delegates for the opportunity to tell you a little bit about what we have been trying to do since your last annual session, and to commend to your appreciation—not myself—but the many fine women in our organization who, being wives of doctors, have given so unstintingly to our work—and *yours*.

Respectfully submitted,

MRS. WILLIAM R. RICHARDS, *President*,  
C.S.M.S. Woman's Auxiliary

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## OBITUARY

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### **Norman N. Smith, M.D.** **1900-1966**

Dr. Norman N. Smith died on March 12, 1966 at the age of 65, at the Hospital of St. Raphael. He was born in New Haven and after graduating from the Yale Scientific School in 1921 and the Yale Medical School in 1924, he interned at Bellevue Hospital in New York City. He was in general practice for several years, during which time he developed a large following. In 1940 he decided to specialize in Otolaryngology, Rhinoplasty and other plastic surgery. After his three year residency at Bellevue Hospital he returned to New Haven to practice his specialty.

He was past president of the American Otorhinological Society, a Diplomat of the American Board of Otolaryngology, a Member of the Society for the Advancement of Reconstructive Surgery, a fellow of the International College of Surgeons, and a member of the Connecticut State Medical Society.

Dr. Norman Smith left his wife, the former Lillian Riemer, a daughter, Mrs. Symmee Stroh of Orange, a son Dr. Robert, of Kalamazoo, Michigan, a sister, Mrs. Sylvia Alpert and a brother Benjamin D. Smith of New Haven, and three grandchildren.

He was a keen student of medicine in his chosen field and showed great surgical skill. He contributed a great deal to the practice of Otolaryngology in New Haven. He will be greatly missed by his family, friends and colleagues.

SAMUEL J. SILVERBERG, M.D.

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## In Memoriam

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**Costello, Henry N.**—Madison; Johns Hopkins Medical School, 1910. Dr. Costello was medical examiner for the town of Hartford for 20 years. He was a member and past president of the Hartford County Medical Association. He was also a member of the Connecticut State Medical Society and the American Medical Association. Dr. Costello died April 8, at the age of 82.

**Schiavetti, Alfred**—Stafford Springs; Tufts Medical School, 1930. Dr. Schiavetti was a practicing physician in the Stafford Springs area for thirty years. He was former chief surgeon at the Johnson

Memorial Hospital, town health officer, town medical examiner, and a trustee of the Mansfield State Training School. He was a member and past president of the Tolland County Medical Association. He was a member of the Connecticut State Medical Society, the American Medical Association, and the American Society of Abdominal Surgery. Dr. Schiavetti died April 14, at the age of 61.

**Tiebout, Harry M.**—Greenwich; Johns Hopkins School of Medicine 1921. Dr. Tiebout, who had practiced in Greenwich for many years, gained world wide fame for his early studies in alcoholism. He was one of the first psychiatrists to give his whole-hearted endorsement to Alcoholics Anonymous as an agent for recovery from alcoholism, a condition he termed a disease of the body, mind and spirit. Dr. Tiebout was a member of the advisory panel on mental health and alcoholism for the World Health Organization in Geneva from 1954 to 1959. Dr. Tiebout had been a trustee of Alcoholics Anonymous since 1957, former national president of the National Committee on Alcoholics, chairman of the American Psychiatric Association Committee on Alcoholism, vice-chairman of the Connecticut Commission on Alcoholics, president of the Connecticut Society of Psychiatry and Neurology, president of the New York Psychiatric Society, and president of the Society of Psychopathology and Psychotherapy. Dr. Tiebout was a Fellow of the American Orthopsychiatric Association. He was a member of the American Medical Association, the Connecticut State Medical Society, and the Fairfield County Medical Association. Dr. Tiebout died April 2, at the age of 70.

**Wise, Raymond T.**—New Britain; New York Medical College, 1944. Dr. Wise was a prominent internist in the New Britain area for many years. During World War II, he served as a lieutenant in the Navy Medical Corps. Dr. Wise was director of medical services at New Britain Memorial Hospital, chief of medicine at Bradley Memorial Hospital, Southington, and attending cardiologist and internist at New Britain General Hospital. He also was the medical examiner for the town of New Britain for the past three years. A Fellow of the American College of Physicians and president of Conton Honor Society of the New York Medical School, he was past president of the New Britain Medical Society and a director of the Hartford County Medical Association and the Connecticut Heart Association. He was a member of the New Britain Medical Society, the Hartford County Medical Association, the Connecticut State Medical Society, and the American Medical Association. Dr. Wise died March 23, at the age of 44.



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# WOMAN'S AUXILIARY

*President*

Mrs. William R. Richards, Hamden

*President-Elect*

Mrs. John D. O'Connell, West Hartford

*First Vice-President*

Mrs. James F. Jones, Danielson

*Second Vice-President*

Mrs. Ralph T. Tella, Stamford



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Mrs. Nicholas Creaturo, Trumbull

*Corresponding Secretary*

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## WOMAN'S AUXILIARY TO THE AMERICAN MEDICAL ASSOCIATION, INC. PRE-TEEN AND TEEN-AGE CONVENTION PROGRAM

**June 27 - July 1**

**Headquarters: Knickerbocker Hotel, Chicago—Champagne Room  
E. Walton Place, Across From Drake Hotel**

### **Monday, June 27—9:30 A.M.-4:30 P.M.**

*Pre-Teens (ages 6-12). Chicago Highlights*—This exciting day starts with a visit to the spectacular Museum of Science and Industry. This 14-acre wonderland features thrilling push-button displays of the latest developments in science and industry. Go aboard a U-505 submarine, explore a real coal mine, make a TV telephone call, and enjoy dozens of other action-packed exhibits. After lunch, see Chicago from the city's tallest observation tower at the Prudential Building. Top off the day with a tour of one of Chicago's famous daily newspapers.

*Teen-agers. Scenic Boat Cruise and Grant Park*—An exciting two-hour cruise on fabulous Lake Michigan and the Chicago River. Bring cameras along to snap the breathtaking panorama of Chicago's famous shoreline and outstanding sights—Chicago Locks, Navy Pier, Grant Park with its museums and Buckingham Fountain, and the Coast Guard Station. Then on to Grant Park for an afternoon of lunch and tours of Shedd Aquarium, the world's largest, and the fascinating Field Museum of Natural History.

### **Tuesday, June 28—9:30 A.M.-4:30 P.M.**

*Pre-Teens. Scenic Cruise and Grant Park*—Same as teen-agers above.

*Teens. Chicago Highlights*—Same as pre-teens above but after lunch, see the sights of Chicago from the outdoor observation deck of the world's tallest apartment skyscraper, the 60-story Marina City built "in the round". Top off the day with a tour of one of Chicago's famous daily newspapers.

*All inclusive price with lunches for Monday and Tuesday \$19.00*

### **Wednesday, June 29—9:30 A.M.-4:30 P.M.**

*Pre-Teens. Town and Country Day*—Start the day with a choice of a special custom designed tour of the famed Art Institute's Junior Museum or the new Borg-Warner Science Hall, featuring mechanical do-it-yourself exhibits, the rotating galaxy wall with exploding stars and highlighting the special Environmental Chamber where you will actually feel chilling cold and desert heat, smell the odors of food, animals and plant life as you watch changing scenes of an 11 minute film! We spend the afternoon in the country at Brookfield Zoo, America's most unusual zoo where moats instead of bars separate the animals from the people and where you will also see the Seven Seas Panorama, a delightful porpoise show. \$10.00.

### **Wednesday, June 29—8:00 A.M.-4:00 P.M.**

*Teens. All Around the Town*—you are special guests of Chicago's notable Don McNeil Breakfast Club radio show; then on to a tour of Chicago's world renowned Police Academy including its communications center and crime lab. Lunch in Chinatown and then an afternoon at the Art Institute with a special tour and the Borg-Warner Science Hall (see pre-teens above). \$10.00.

### **Thursday, June 30—9:30 A.M.-4:30 P.M.**

*Pre-Teens. Sightseeing and Gala Swim Party*—Visit a TV show or studio and on to a special tour of the Chicago Historical Society for a visit to the

Lincoln section; see his personal letters and other momentos of Lincoln's Life: A gala afternoon . . . pre-teens join teens for a barbecue lunch and swim party. \$10.00.

**Thursday, June 30—9:30 A.M.-4:30 P.M.**

*Teens. Sightseeing and Gala Swim Party*—A morning tour of the Board of Trade where the action reaches fever pitch. Then on to a gala afternoon . . . a barbecue lunch and swim party at the famed Edgewater Beach Hotel. \$10.00.

**Friday, July 1—9:30 A.M.-4:30 P.M.**

*Pre-Teens and Teens. Great Lakes Naval Training Station*—A fabulous day at the world's largest naval training base. See graduation exercises, a parade review and take a ride on a naval cruiser. \$10.00.

**EVENING ACTIVITIES**

**Monday, June 27**

Teens and all children over the age of 10 (teens will be in their own group)

**7:15 P.M.-11:30 P.M.**

*Smorgasbord feast and Kismet*

**Teens: 7:30 P.M.-12:15 A.M.**

A memorable evening at the world renowned Kungsholm Restaurant. A lavish Smorgasbord feast and then on to the internationally acclaimed Kungsholm's Miniature Grand Opera Theater for a performance of the famed Broadway hit, *Kismet*, featuring the original cast of Alfred Drake and Doretta Morrow. \$10.95.

Pre-teens will take an excursion before the show to see the famed colored Buckingham Fountain Water Display. Teens will follow the theater performance with a tour of Chicago at night.

*Pre-Teens.* (For 10 and under or those not attending above)—Dinner and a suitable film \$10.00.

**Wednesday, June 29—7:30 P.M.-12:00 P.M.**

*Teens. A Night in Old Town*—An exciting evening in Chicago's intriguing section known as Old Town, a glamorous version of New York's Greenwich Village. Dinner at Paul Bunyan's—family style—and then on to two shows featuring folk and rock'n roll entertainment. \$11.25.

**7:00 P.M.-11:00 P.M.**

*Pre-Teens.* Dinner and entertainment at the Knickerbocker Hotel. \$8.75.

**RESERVATIONS**

Make in advance if possible. Right to close out reservations by June 18 reserved by committee.

Write to Gulliver's Trails, 25 Central Park West, New York, N.Y. 10023. Check enclosed will confirm reservation.

## BOOKS RECEIVED

*Books received for review are acknowledged in this department and such acknowledgement must be regarded as a sufficient return for the courtesy of the sender. Selection will be made for review in the interests of our readers and as space permits.*

*Community Mental Health Services In Northern Europe.* Great Britain, Netherlands, Denmark, and Sweden. By Sylvan S. Furman. U.S. Dept. of Health, Education & Welfare, Public Health Service, National Institutes of Health, National Institute of Mental Health, Bethesda, Maryland, 20014. 1966. 215 pp. Price not specified.

*Medical Pharmacology.* Principles and Concepts. Third Edition. Andres Goth, M.D. The C. V. Mosby Co., St. Louis, Missouri, 1966. 668 pp. \$12.50.

*Disorders of Carbohydrate Metabolism in Infancy.* Volume III in the Series Major Problems in Clinical Pediatrics. Marvin Cornblath, M.D. and Robert Schwartz, M.D. Alexander J. Schaffer, Consulting Editor. W. B. Saunders Co., Philadelphia and London, 1966. 297 pp. Illustrated. \$8.50.

*Five Congenital Cardiac Defects.* A study of the Profile and Natural History. American Heart Assoc. Monograph Number Twelve. 17 Contributors. Distribution Department, American Heart Assoc., 44 East 23rd Street, New York, N.Y. 10010. \$2.50.

*Transcultural Psychiatry.* Ciba Foundation Symposium. Edited by A. V. S. de Reuck and Ruth Porter. Little, Brown and Company, Boston, 1965. 396 pp. with 10 illustrations. \$12.00.

*Preimplantation Stages of Pregnancy.* Ciba Foundation Symposium. Edited by G. E. W. Wolstenholme and Maeve O'Connor. Little, Brown and Company, Boston, 1965. 430 pp. with 153 illustrations. \$13.50.

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George J. Geanuracos, M.D., Paul V. Leone, M.D., John F. McGarry, M.D. and Morris P. Pitock, M.D., announces the removal of their offices to 50 Ridgefield Avenue, Bridgeport.

Joseph R. Gionfriddo, M.D., announces the opening of an office for the practice of radiology at the Cedar Lake Medical Center, New Britain.

Charles T. Meacham, M.D. and Thomas J. Walsh, M.D., announce the removal of their office for the practice of ophthalmology to 1911 Summer Street, Stamford.

Erwin D. Niesyn, M.D., announces the removal of his office to 50 Ridgefield Avenue, Bridgeport.

Robert L. Rackliffe, M.D., announces the opening of an office for the practice of pediatrics at 670 Arch Street, New Britain.

Louis F. Raymond, M.D., announces a new location of his office for the practice of diseases of the eye and eye surgery at 139 Danbury Road, Ridgefield.

John L. Sullivan, M.D., Nicholas P. Gill, M.D. and James M. Alexander, M.D., announces the removal of their offices to 50 Ridgefield Avenue, Bridgeport.

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## AROUND THE STATE

### 182nd Annual Meeting New Haven County Medical Association March 24, 1966

The 182nd Annual Meeting of the New Haven County Medical Association, held at the Waverly Inn, Cheshire, Conn., was called to order at 3:30 P.M. by the President, Dr. Luca E. Celentano.

Our Woman's Auxiliary met simultaneously to enjoy an especially arranged program which featured flower arrangements by Mr. Frederick Sternberg of "Flowerland". Both groups joined later for a social hour and dinner.

During the business session guests and delegates from other county associations were introduced, committee reports were read and a slate of officers for 1966-1967 was elected as follows:

President: Max Caplan, Meriden

Vice-President: Bernard A. Burnham, Waterbury

Clerk: H. A. Levin, New Haven

Councilor: Frank A. Abbot, Waterbury

Associate Councilor: Stewart Petrie, Derby

Kurt Pelz, Wallingford

Member, Executive Committee: Luca E. Celentano, New Haven

During the evening Mrs. John Mendillo, representing the Woman's Auxiliary presented their annual report for Mrs. Arnold Baskin.

A gift and congratulations to Dr. Anthony J. Mendillo on the occasion of his 80th birthday, the presentation of the out-going President's Plaque to Dr. Luca E. Celentano, and the inauguration of Dr. Max Caplan of Meriden, as the Incoming President, were highlights of the dinner hour.

The evening program was completed by Shearen Elebash who was presented by Dr. Charles Verstandig, Chairman of the Program Committee. His varied program of music, recitations, and whimsicalities was enthusiastically received by the large audience.

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## NEW BOOKS IN REVIEW

**LEOPOLD'S PRINCIPLES AND METHODS OF PHYSICAL DIAGNOSIS. Third Edition. By Henry U. Hopkins, M.D., W. B. Saunders Co., Philadelphia and London, 1965. 503 pp., 339 figures. \$8.50.**

Reviewed by: LOUIS H. NAHUM

The author was a pupil of Leopold, is now professor of Clinical Medicine at the University of Pennsylvania School of Medicine and agreed to complete the third edition at the request of Professor Leopold's family. Obviously one would expect many changes from the second edition and there are.

The philosophy underlying the book is that one must carefully listen to the patient's story then carefully examine the patient and then only seek such ancillary studies as then seem essential to confirm the tentative diagnosis or alternate diagnoses derived from physical diagnosis. The book succeeds beyond measure in providing an introduction into the basic procedures of history taking and the performance of a physical examination.

It states clearly what should be done, how it should be done and why. It clearly defines the findings that would be considered within the normal range in a healthy person. Some of the innumerable variations found in disease are mentioned. What is more important is the success the author has achieved in helping the student correlate the abnormal findings with the underlying physiologic and pathologic changes responsible for them.

One can tell that the author has delved deep into his own personal experience from contacts with students over many years. It is highly recommended to students and physicians alike.

The figures are clear, the printing is high class. Only one error was noted—Fig. 159 is upside down.

**TRACY'S THE DOCTOR AS A WITNESS William J. Curran, W. B. Saunders Co., Philadelphia and London, 1965, 196 pp. \$5.75.**

Reviewed by: LOUIS H. NAHUM

There are at least two ways in which a doctor becomes unhappy in a court of law. One is the idea of gamesmanship involved in the advisory process. The doctor is not accustomed to this and prefers to be a neutral witness not a partisan one and is irked when he is forced into the latter role. The second is when he lacks preparation for the case by previous conferences with the attorney and the maintaining of accurate notes and exhibits to support his opinion.

This second edition by Professor Curran of the late Dr. Tracy's First Edition is a completely new book. It explains the advisory process. It advises on the preparation of medical reports for attorneys. It analyzes testimony on "pain and suffering" in personal injury cases. It deals with demonstrative techniques, photography, X-rays, and discusses the direct and indirect attack methods on the testimony of a medical expert witness.

There is a new section on legal aspects of experimental methods and clinical investigation. A chapter on medical

malpractice with litigation included. There is specific advice on courtroom testimony for the various specialists in medicine and for the general practitioner. The whole effort was performed by Professor Curran after personal interviews with 34 prominent physicians, attorneys, and the judiciary.

The book is comprehensive and should be in the possession of every physician who is ever called upon to report to an attorney or to testify in court.

**TRAUMA TO THE LIVER. By Gordon F. Madding, M.D. Vol. II in the Series Major Problems in Clinical Surgery. The W. B. Saunders Company, Philadelphia and London, 1965. 134 pp., illustrated. \$6.00.**

Reviewed by: HUGH F. LENA

This is the third volume in a new monograph series, Major Problems in Clinical Surgery, the first two being Child's THE LIVER AND PORTAL HYPERTENSION, and Welch's POLYPOID LESIONS OF GASTRO-INTESTINAL TRACT. The average general surgeon probably does not have a wide personal experience with liver injuries in spite of the fact that these injuries are increasing. The authors of this monograph have had a longstanding interest in these problems, beginning during the Second World War, when they were members of the Second Auxiliary Surgical Group.

The chapter on Surgical Anatomy is very useful. From a surgical standpoint, the area where the falciform ligament joins the liver is not the actual demarcation between the left and right lobes. The main fissure dividing the organ into two lobes actually runs between the fossa of the inferior vena cava posteriorly and the fossa of the gall bladder anteriorly. The quadrate lobe makes up most of the medial segment of the left lobe. The intra-hepatic arrangements which are often neglected in the standard anatomy textbooks are presented in detailed form. Surgical interest in major liver resections require a familiarity with these facts.

A brief historical review of the treatment of liver injuries is given with the addition of new developments during the Second World War. During a 16 month period, there were 3,154 patients with abdominal and thoracico-abdominal wounds and 829 wounds of the liver were included. The mortality rate was 27 per cent in contrast to an overall mortality rate of 66 per cent in the First World War. The decreased mortality was thought to be due to routine operations in all cases, abandonment of packing, universal use of drainage, proper timing of surgery and more liberal use of blood.

The classification and diagnosis are discussed thoroughly. The management is presented clearly and concisely. The surgical techniques employed in the repair of all types of hepatic damage are described in detail. Pre- and postoperative care is especially well presented. All major complications are found in this monograph and the important principles useful in avoiding these complications are stressed.

The last chapter is devoted to liver hemostasis and this includes an historical review.



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The illustrations are most helpful in understanding the technical descriptions. This monograph is an excellent review of liver trauma and would be a useful addition to a surgeon's library.

***SURGERY IN AMERICA. From the Colonial Era to the Twentieth Century. Edited by A. Scott Earle, M.D., W. B. Saunders Co., Philadelphia and London, 1965. 269 pp. Illustrated. \$8.50.***

Reviewed by JAMES R. CULLEN

This history of *Surgery in America* actually covers the era of surgery from the Colonial days to the twentieth century and does not include surgical events which have transpired since 1900. Another book is in preparation, which together with this one, will bring a very comprehensive account of the development of surgery on this continent from the Colonial era to the present century. This text includes the classics of American surgical writing, such as McDowell's papers on ovariectomy and Warren's and Bigelow's accounts of the first use of ether for surgical anesthesia. Representative writings of men such as Philip Syng Physick, John Syng Dorsey and John Jones are included because their teachings and writings helped shape the course of surgery from its very onset in this country. Many of the topics covered have been edited by other authors, including H. A. A. Beach's selections from the early surgical records of the Massachusetts General Hospital and Robert Buck's annotation of a colonial apprentice's diary. Again other subjects have been selected because of the great feats of surgery about which they tell, including Valentine Mott's *tout de fource*, the ligation of the innominate artery in 1818, and Nathan Smith's ovariectomy performed soon after McDowell's. These operations on this continent, which were performed while European surgery was at its peak, foretold the boldness and ingenuity that was to characterize American surgery in the years ahead.

Altogether there are twenty-four different historical topics covering 269 pages in this book. The titles are most interesting, ranging from "Tucker's Wife's Leg" by Robert W. Buck through a "Case of Extra-Uterine Foetus" by John Bard. John Jones' "Introductory Lecture to His Course in Surgery," "Excerpts from a Military Journal During the Revolutionary War" by James Thacher, the "Remarkable Case of the Swallowing of a Silver Spoon" by Samuel White, "Extracting Poisonous Substances from the Stomach" and "The Use of Soluble Sutures in Surgery" by Philip Syng Physick. Also, McDowell's writing on his "Extirpation of Diseased Ovaria and Observations on Diseased Ovaria," "The Training of the Surgeon" by William Stewart Halsted, "Case Reports of the Massachusetts General Hospital Before 1846" and "Insensibility During Surgical Operations Produced By Inhalation" by Henry Jacob Bigelow are interesting articles. Many of these topics are from the authors' own hand-written case abstracts, such as the "Excerpts from William Beaumont's Journal" by William Beaumont, with a presentation of the material which is delightfully interesting to read.

The author of this book states that, in selecting the writings to make up this volume, he has "attempted to maintain as high a level of readability as possible" and a short perusal of any one of the excerpts will readily show that he has attained this objective. The book is so readable

that it is difficult to put aside once one begins to read any of the articles. I recommend this book to all surgeons and to all physicians who are interested in the history of surgery during this early period. One of the great objectives that it has accomplished is that it gives a picture of the distance which American surgery has travelled during the years required for its founding and growth in this country and also an appreciation of the debt which surgeons of today owe to the men of their profession who carried the art and the science of surgery forward over the years.

***PRINCIPLES OF CHEST ROENTGENOLOGY. By Benjamin Felson, M.D., Aaron S. Weinstein, M.D., and Harold B. Spitz, M.D., W. B. Saunders Company, Philadelphia, Pa. and London, 1965, 221 pp., 150 Roentgenograms on 131 Figures, \$6.00.***

Reviewed by: ROBERT M. LOWMAN

The authors have utilized the programmed learning approach to present logically organized procedures. The authors have utilized roentgenograms of commonly encountered diseases to demonstrate various points. The introductory chapter is utilized to explain the various roentgenographic procedures used in the examination of the chest. Chapters on the roentgen examination and the normal anatomy of the lung follow.

Subsequent chapters deal with various entities concerning the silhouette sign, the air bronchogram, the signs of lobar and segmental collapse, pleural effusion and extrapleural disease. A special chapter has been included in the volume to discussing the causes of rib notching. The final chapter represents a self test quiz on ten selected cases in an attempt to measure the ability of the reader to apply the principles.

A word of caution concerning the technic of programmed instruction should be enforced here. As one reads the material, the reader notes that it is systematically arranged and is presented in small, simple, learning steps. Because the purpose is to teach rather than to just present information, items are often repeated in different forms and in different context. What will appear as needless repetition in other presentations of reading material is done here to reinforce the learning process.

The authors have assumed the unusual task of presenting information utilizing the programmed learning technic. Because it represents a forward look in teaching process in radiology, it deserves critical consideration.

It is important to point out that this kind of programmed review is not intended as a substitute for extended reading or study. It is possible that this programmed text can serve as a very satisfactory introduction to the study of the very excellent volume for diseases of the chest offered by Felson.

This is a good text. The format is pleasant, the material is legible and ably presented. It is well designed and clearly written. The illustrations are most adequately presented.

The authors are to be congratulated on their effort. A plea to encompass some of the effort in any forthcoming edition by Felson is hoped for. It is hoped that this effort will be the stimulus to initiate other authoritative groups in radiology to undertake similar efforts.

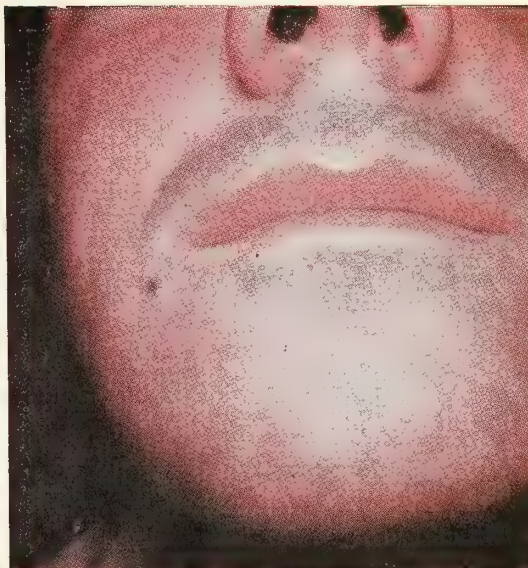


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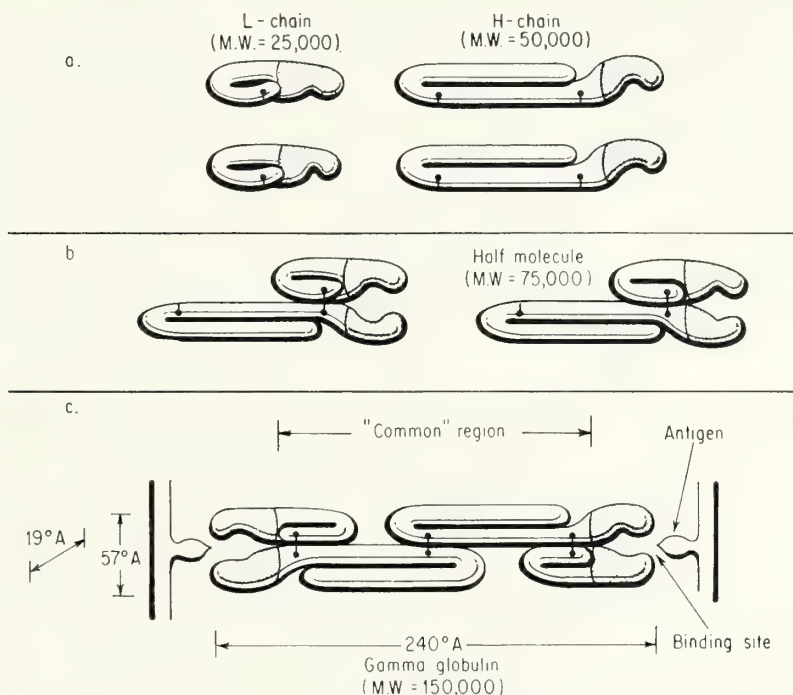


# Connecticut Medicine

Connecticut State  
Medical Journal

Vol. 30 / June, 1966, / Number 6

**CANCER ISSUE: I. Henry M. Williams, M.D., Guest Editor**



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ANTIBODY MOLECULES OF GAMMA GLOBULIN (see page 381)

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# Connecticut Medicine

## editorials

### Recognizing Cytostructural Changes

The internist has practiced cytostructural diagnoses for almost a century, especially in hematology. More recently cellular constitution of inflammatory exudates has revealed abnormalities not in the character of the cells but in the relative proportions in which normal cells appear in the field of inflammation as in ulcerative colitis or interstitial cystitis. Furthermore, our concepts of a disease can be greatly improved when it can be recognized in its cytostructural characteristics of individual cells. In this way the disease can be discovered early and perhaps its etiology unravelled. The vaginal cytogram is an example when hormonal deficiency can be quickly recognized.

Neoplastic disease which is everywhere recognized as a cytopathology is invariably associated with characteristic cytostructural features. Studies in carcinogenesis in the laboratory indicate that these features are present from its outset. There are changes in membrane structure which lessen adhesiveness and increase cell permeability. Cytoplasmic changes occur in the endoplasmic reticulum and the disposition of the organelles. There are changes in the nucleus, such as nucleolar-cytoplasmic and nucleolar nucleus size ratios as well as in the disposition and aggregation of chromatin. Finally there are changes in the DNA-RNA ratio of the cell.<sup>1</sup> The Papanicolaou staining method was de-

signed to highlight these features of all neoplastic populations regardless of etiology.

Papanicolaou spent his lifetime elucidating features of cancer of the cervix. But presently available techniques permit the use of cytological techniques in a wide spectrum of neoplasms besides those of the cervix—including those of the corpus uterus, lung, stomach, pancreas, colon, rectum, bladder, prostate and oropharynx.<sup>2</sup> Thus cytological methods for the diagnosis of cancer can be applied to surveillance of well populations. Cancer of the cervix, corpus uterus, oropharynx, fall into this group. Less reliable is recognition of cancer of prostate and of lung.

Besides the search for cancer in well populations, cytological methods especially help in early diagnosis of clinically suspected neoplastic disease. It is a better method than small biopsy sampling which may not reveal presence of invisible cancer loci in a large area of mucosa. If the lesion is visible of course, biopsy can add vital information regarding the depth of invasion and character of the neoplastic growth.

The accuracy and reliability of cytostructural diagnosis depends upon how well the specimen is taken and handled. The closer the sample of cells is taken to the locus of their origin, the richer it will be in its proportion of abnormal elements. For example in cancer of the cervix the disease is ordinarily near the squamous-columnar junction. It is here the scraping should be taken making sure to avoid contamination by hemorrhage. Optimally

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this means taking the specimen between 10-20th day of cycle. It also means the vagina must also be free of lubricants, jellies and douches.

Dryness deforms cells, and this demands that a thin, even smear should immediately be immersed in a fixative. Furthermore, the pathologist reading the smear should be experienced in cytologic interpretations because this is open to many errors of omission and commission. With these safeguards a properly taken cervical scrape is sufficient for diagnosis even if a biopsy taken is found to be negative.

Brennan points out that cancer of the cervix is responsible for 10,000 deaths a year and believes that this can be reduced to 1 per cent or less of its present rate by routine use of vaginal cytologic examination. At the cancer detection clinic in Detroit they found six cases per thousand in white and twice this in Negro women and 90 per cent were found on the first examination. The high risk subgroups were the multiple married, the early married and the very poor. This recognition by routine cytological diagnosis that cervical cancer can occur quite early is changing our concept of this disease.<sup>3,4</sup> We have here a highly reliable procedure for the detection of the third most common cause of cancer in women and all we need is to extend this method in the routine examination of women.

Formerly few diseases could be arrested and fewer still reversed to allow complete repair and return to fully normal health, because chronic diseases could not be identified before onset of organ failure. Nearly all our curable patients are among those who are not yet sick, are symptom free, functionally well, but who bear at a stage of "incipiency" a disease process apparent only at the cellular level or chemical pathology. This is true not only of neoplastic disease, but of all the major systemic diseases which are not of bacterial etiology.

Thirty years ago clinical medicine was largely based upon an applied physiology which tried to explain disease from the experimental study of induced organ deficiency and whole organ function. Modern biology and scientific medicine is working towards explanation of disease in terms of cellular and subcellular processes. What we are now searching for is the stage of presymptomatic and genuinely curative medicine. The cytology technique, the two-hour post-prandial blood sugar, the search for hypercholesterolemia, hyperuricemia, and hormonal disturbances, are examples of this trend. We may expect that this trend will improve medical practice by perfecting the art of diagnosis in all the fullness and excellence open to us in this particular stage of medical progress.

L.H.N.

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## A Model For Studying Carcinogenesis

The first step in a proposed sequence leading to a radiation induced tumor is a production of a genetic alteration (a somatic mutation) in one or in a number of the irradiated cells. This alteration can be produced by direct action of the radiation on the genetic apparatus of the cell or by an indirect mechanism involving primary damage to extragenetic sites, or activation of a latent virus. All that matters is the result that the genetic apparatus of the cell has been specifically and presumably irreversibly altered. What is not yet known is whether the same mutation occurs in every tumor or whether different alterations lead to different kinds of tumors. In chronic granulocytic leukemia the Philadelphia chromosome is consistently associated with it, but not in other mammalian tumors.

Reasoning further Cole<sup>1</sup> suggests that there may in fact be not a single mutation, but two or more specific mutations in sequence, the first one of which may be inherited. This could explain why it is that only certain strains of mice are susceptible to tumor induction by radiation or other carcinogen. What we still do not know is whether the presumed inherited induction is an essential predecessor of the carcinogenic somatic mutation.

Ionizing radiation does produce mutation and both the dose rate and quality of the radiation, for example whether gamma rays or neutron emissions can influence the frequency of mutations. Cole points out that visible chromosome aberrations do represent mutagenic effects of the radiation and that intra-cellular repair does occur after irradiation from any form. What is not known is to what extent the repair phenomena operate to either enhance or retard the carcinogenic mutation produced by irradiation. What is known is that the killing varies considerably with the cell cycle; but when the cell is most sensitive is not yet settled. Cole obtained information which suggests that a cell during the stage of mitosis both in the liver and kidney is rendered more susceptible to the development of a carcinogenic mutation by ionizing radiation.





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Once a specific mutation has been produced, it is necessary of course that the cell survive with its proliferative capacity intact for otherwise it could not lead to a tumor development. The so-called therapeutic effect of large single doses of radiation on certain tumors can be explained that cells have been killed and few survive so that the number of cells which might give rise to another tumor are reduced and these may not do so because they may not represent actual carcinogenic mutations.

We can thus see that the production of a specifically mutated cell involves several variables. First the genetically altered cell must enter mitosis. This occurs as a natural event in bone marrow, bowel epithelium or skin where mitotic activity is normally present. Injury, infection and certain hormones also increase mitotic activity and could cause a mutated cell to enter mitosis earlier than would otherwise be expected. Cole believes that certain viruses might be carcinogenic through such a mechanism rather than by the production of mutated cells. Even radiation itself by destroying cells in marrow or gut and subsequent regeneration could have a similarly non-specific effect on cell proliferation.

In other organs, cells are dormant for long periods of time without dividing but accumulating mutations as occurs in liver and kidney. If one starts mitosis in such organs as for example by giving  $\text{C Cl}_4$  to destroy liver cells, or by infection, then the mutated cells begin to divide and a tumor may be said to have begun its development. We define a neoplasm then as beginning in a cell which continues to proliferate even when the initial stimulus has been removed. What is needed is a specially mutated cell which is brought to mitosis. There is of course the possibility that the cell is hormone dependent and responding to such or other mitotic stimulus. All this would mean that the stimulus to mitosis if present would increase tumor growth and if eliminated, decrease tumor growth, but it would not restore the mutated cell to normal.

One theory of malignancy and complete autonomy is that the primary cell or cells that have escaped growth control goes through repeated selection from the initial tumor cell population. As additional mutations occur in the population they confer yet further selective advantages on certain tumor cells to survive and grow and that this selection continues throughout the life of the tumor. An example of this is when a second application of a mutagenic agent is applied in later stages of tumor development.

In many instances of tumor development however, no additional stimulation either mutagenic or non-mutagenic is apparent. This could be due to increased mitotic activity itself in the tumor which might account for an increase in spontaneous muta-

tion and tumor progression. Or the genetic change may be sufficient to render the mitotic apparatus permanently unstable so that in every subsequent cell division there would be increased probability of some chromosome rearrangement. In this way there would be more cells in a tumor population with chromosome aberrations and this could increase the opportunity for continued selection of altered cell clones.

Whatever mechanism that operates to produce additional genetic alterations in a given tumor, the net result is that most mammalian neoplasms examined to date in their late stages consist of one or a few clones of cells which are markedly altered genetically. Chromosome studies have indicated that nearly all malignant neoplasms consist of a single or a very few stem lines of cells with a particular chromosome aberration. In granulocytic leukemia the Philadelphia chromosome is present in every case, but otherwise these chromosome aberrations usually vary from case to case. Where repeated studies have been done there has been good evidence for progressive clonal selection within individual tumors.<sup>2</sup>

The final point is that many tumor cells with genetic aberrations produced in the course of tumor progression are recognized by the host as antigenically foreign and eliminated so that immunological factors may be important in this aspect of tumor development. What is not understood as yet is whether the stem-lines which do come to predominate in the fully developed tumor and which almost invariably show marked chromosome aberrations are sufficiently altered antigenically to be so recognized as foreign. The other possibility is that the immunological competence of the host is in some way impaired.

These then represent current concepts on the stages of carcinogenesis following irradiation and can be used as a model for carcinogenesis in general. Somatic mutation can be considered as the final common pathway by which both radiation and viruses initiate neoplasia and chemical carcinogenesis probably act similarly. There are problems of initiation and problems of promotion of all growth. Then there are problems of altered endocrine systems on the tumors being produced and hormone effects upon tumor cell survival.<sup>3</sup> Finally is the problem of antigenicity and body response to the presence of the tumor.

In order to measure the carcinogenic potential of the low doses of radiation, small fractions, and varying dose rates, to which many people are exposed, it will require extension of our present chromosome studies to the sub-chromosomal and perhaps to the molecular level. Even then the post-mutational events in Cole's model will determine

whether a tumor will develop in a particular individual and the possible effects of various environmental factors on these events would have to be investigated. There is little doubt that the model will facilitate investigation in carcinogenesis and help clarify many as yet unsolved problems.

L.H.N.

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## The Maturing Principle And Cancer

The idea that actively proliferating cells require some principle or substance to bring them to maturity and that without this principle a given immature cell might continue to proliferate indefinitely first appeared in 1926 when Minot and Murphy fed patients with pernicious anemia liver with the result that the anemia improved and the bone marrow returned to normal. Before 1926 pernicious anemia was considered by some as cancer of red cells since the bone marrow of such patients was solidly replaced by megaloblasts, the primitive precursor of the erythrocytes. The maturation of these megaloblasts into erythrocytes did not take place and the disease went on relentlessly until death overtook the victims. Liver contained a substance necessary to bring about maturation of megaloblasts, and this substance led to a return of the hematopoietic system to normal. We know now that the maturing substance is  $B_{12}$ .

There is evidence of the existence of a maturing principle for other cells of the blood. Miller et al<sup>1</sup> found myelokinetic acid causes maturation of lymphocytes and lymphokinetic acid causes maturation of myeloid cells. If such substances operate to bring various components of the hematopoietic system to maturity, perhaps maturing principles also exist which cause other proliferating cells of the body to maturity, cells which are usually the ones that undergo malignant change. If the deficiency of a maturing principle leads to abnormal hematopoietic cell proliferation, why can it not be that a similar mechanism operates also in other cells and tissues? If actively proliferating cells cannot come to maturity for lack of a maturing principle, it is not difficult to imagine that such cells could continue proliferation indefinitely and produce a cancer. This hypothesis has been proposed recently by

Herbut et al<sup>2</sup> and should lead to experiments designed to isolate maturing principles for various normal cells and determine whether or not they are absent in cancer of these cells.

Generally cancer follows a relentlessly progressive course to the death of the patient. But this is not always so. Everson and Cole<sup>3</sup> in a preliminary report stated that over 600 cases of recovery from cancer have been reported and of these 47 were thoroughly documented and unequivocal in patients suffering from cancer arising in almost every organ of the body. Herbut et al<sup>2</sup> have reported a thoroughly documented case of cancer of the stomach in a 56 year old male who at operation showed widespread metastases, who was closed up to die and who recovered after the operation. The tumor of which the authors have histologic sections regressed and the patient was well 15 years later. What could have happened to change this patient from being cancer susceptible to cancer resistant? Up to the present time the course of recovery in the extremely rare instance reported above remains a complete mystery. There are however animals, like the guinea pig whose serum contains a powerful tumor inhibitory principle TIP against a variety of transplantable tumors from whom perhaps we may get clues to the mystery.<sup>4,5</sup>

Herbut et al<sup>2</sup> have carefully scanned all the organs of the guinea pig and found that only the liver contains it and that in the blood it is bound up with the globulin fraction. TIP is not however peculiar to the guinea pig but is also present in other mammals albeit to a lesser degree. The normal human liver also produces T.I.P. which it imparts to the blood stream and also to the bile. What is not known and needs study is whether T.I.P. declines in amounts or disappears in the patient who develops cancer. What is also not known is what influence is exerted on T.I.P. by the numerous agents and factors that have been associated with the production of cancer such as enzymes, viruses, bacteria, fungi, various chemicals, hormones, rays and hereditary factors. T.I.P. could act as an anti-tumor agent or it could be a maturing principle operating to bring proliferating cells to maturity, thereby preventing excessive proliferation. It is obvious that we have here several hypotheses, that it is to be hoped will lead to further experiments to test their validity. Herbut et al<sup>2</sup> suggest that the maturing principle and T.I.P. may be one and the same substance. Even if the hypothesis prove wrong, in the verification process, it may be expected that much useful knowledge will result from the attempt at elaboration of this theme.

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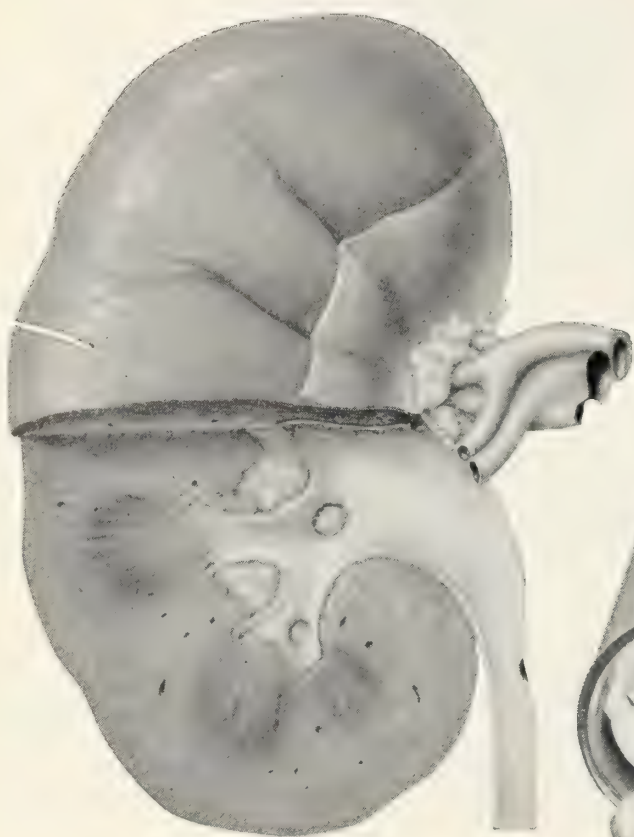
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- From knowledge thus acquired might come clues to the development of new therapeutic agents of significant value to the physician.

For example, the Renal Research Program put fifteen years into this search before chlorothiazide became available. But because these years had first led to a greater understanding of basic problems, the desired criteria for chlorothiazide existed before the drug was developed.

Along with other research teams at Merck Sharp & Dohme, the Renal Research Program continues to add new understanding of basic problems—understanding which will lead to important new therapeutic agents.

**MERCK SHARP & DOHME** Division of Merck & Co., Inc., West Point, Pa.

**where today's theory is tomorrow's therapy**



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## Nursing The Patient With Cancer— An Exercise In Timing

To everything there is a season. We find rhythms and patterns in nature and in our lives and feelings. Nowhere is it more important to match the ebb and flow of hope and despair with understanding and encouragement than in the nursing care of the patient with cancer.

There Is a Time to Know—Contrary to some opinion, cancer is an illness that is not dull, routine or easily nursed by the mediocre among us. The phrase “just keep him comfortable” is, and should be, extinct. In this changing field there are always new developments to interest the alert nurse. The status of mammography and the self-obtained cervical cytology specimen are subjects that patients, their families and our own friends ask us about. We must understand postoperative care following extensive surgery, the side effects of chemotherapy and safety precautions required when radiation medicine is used. In cancer nursing, there are abundant opportunities to contribute to the patient’s motivation and adjustment, and we must realize that these goals are influenced by things as basic as odor control and skin care and that the methods of achieving them also change and improve.

Learning to know ourselves is vital too, for how we perceive cancer and how deeply we feel about any patient as a person rather than “another mastectomy,” creates in part the climate we work in and affects the feelings of everyone around us. The point about knowledge is that it gives both the patient and the nurse confidence and confidence is the first brick in the wall of support.

There is a Time for Silence—In our anxious groping for the right word we are sometimes oblivious to the value of the right silence. Not just in illness, but in all other crises in life, the principle pro-

tagonist may be so enmeshed in complex problems and so close to despair that ordinary verbs and adjectives cannot approach the intensity of his concern. Far better than resorting to clichés, or a torrent of well meant words, is to remain quiet, for though silence is sometimes callous, it is as often companionable and therapeutic. Silence and some people are especially compatible. Just as some people are not joiners, some patients are not garrulous.

We might examine our uneasiness with silence, our compulsion to advise others, to answer them, to decide for them. The patient or family member who says “What shall I do?” or “What do you think?” is often making a statement and not an inquiry. He is trying to convey his need to talk out his concerns. We can help him to do this by our understanding silence.

There is a Time for Speech—There is, in cancer, the most pressing need for doctors and nurses to talk to each other, and yet something so important does not always occur. Nurses often under-rate the value of their observations, nor do they always report them accurately. In a case conference, they are reluctant to speak. It is also true that doctors don’t always tell us whether their patients know they have cancer, or what they understand of the prognosis, but we compound the error when we don’t request this information.

Curiously, we don’t always recognize the occasions when patients and their families need not a speech, but a few words of reassurance. As people wait—for X-rays, or report of a biopsy, or a relative’s return from surgery—their fears mount and the minutes drag. This is not the time to rush by them. It is, rather, a time to clarify, to interpret. A misunderstood term or a false notion of the time required for surgical procedures may be causing needless concern. A simple “I’m sorry” or “Is there something I can do for you?” will reduce their feelings of isolation and anxiety.

There is a Time for Understanding—The cancer story, so old to us, is always new and devastating to the patient. To this illness, so fraught with gravity, he brings his old problems and weaknesses. We can help him by recognizing rather than belittling his situation and by remembering that all patients are individuals, with varying degrees of illness and maturity, with different backgrounds and sources of emotional support. We can help the patient most of all by our own attitudes, so readily perceived and quickly reacted to by him, for these transcend words.

VIRGINIA BARCKLEY, R.N.

Nursing Consultant for the American Cancer Society.

## *In Memoriam*

Ralph E. Kendall, M.D.,

Edward J. Ottenheimer, M.D.,

Donald A. Bristoll, M.D.

*"And Elihu answered and said, I am very young and ye are very old, wherefore I was afraid and durst not show you my opinion.—But there is a spirit in man, and the inspiration of the Almighty giveth them understanding.—Therefore I said: hearken to me; I also will shew my opinion."*

*(The Book of Job)*

Reviewing the collective worth of the three physicians commemorated by this Special Cancer issue of CONNECTICUT MEDICINE, I am awe struck but proud to have selected a similar vocation. At one and the same time, the sheer breadth of their accomplishment does great honor to Connecticut while intimately touching the lives of so many individually.

Throughout the twelve years of our friendship, for example, Ralph Kendall became more than a teacher; above all he was my friend, a second father, a constant source of wisdom, perspective and inspiration. I must summon the great words of the past, said by men for whom Medicine was not a vocation, but a religion, to pay just tribute to this great yet humble man, and to his two colleagues, Dr. Ottenheimer and Dr. Bristoll: For these three, whilst ever devoted to the marriage of science and truth, at the same time gave unstintingly of the supreme gift of love to all who sought it out.

I sorrow, too, that in 1966, our beloved Edward Meiss retires after years of selfless devotion as active Executive Director of the Connecticut Division, American Cancer Society. Without his unflagging efforts, our Connecticut Division could not have thrived as it has. Continuing in the tradition of service and self-sacrifice established by these four men surpasses responsibility: it is a sacred trust of our generation. And we durst not stumble.

The following paragraphs, written by Edward Meiss to me a short time ago, convey quite unconsciously that behind his quiet, tactful, helpful ways lay a huge fund of wisdom and his most loveable quality of genuine humility.

"This special cancer issue of CONNECTICUT MEDICINE is dedicated to the memory of three outstanding physician leaders in Connecticut's cancer control effort, all of whom died within a brief time of each other in late 1963 and early 1964.

They are Dr. Edward J. Ottenheimer, of Windham, Dr. Ralph E. Kendall, of Hartford and Dr. Donald A. Bristoll, of New Britain. Each gave leadership to the establishment of Connecticut's cancer records and the development of the American Cancer Society in Connecticut. Their interest in research was exemplified by Dr. Kendall's early championship of the Pap smear, which led to the sponsorship by the Cancer Society of what was to become one of the country's largest cytology training and service centers in Hartford.

But in a very real sense this issue is a tribute to all that small band of physicians who were the dedicated leaders of cancer control in Connecticut and who have died in the intervening years. Most served as Presidents of the American Cancer Society, Connecticut Division. All were completely devoted to the quest for a cure for cancer. Their efforts were an inspiration to all who worked with them.

Among their number were Dr. A. N. Creadick, Dr. George M. Smith, Dr. Samuel C. Harvey, Dr. Creighton Barker, Dr. Ashley W. Oughterson, all of New Haven; Dr. Alfred L. Burgdorf, Dr. Philip McLellan, Dr. R. Starr Lampson, Dr. Douglas J. Roberts, Dr. Donald Wells, of Hartford.

Their devotion is reflected in the standing of Connecticut as a leader in the work being carried on against cancer."

We can bestow no greater honor upon these men than the admiration of their colleagues and an avowed dedication to continue their work. The special issue of CONNECTICUT MEDICINE, I hope, will demonstrate that there has been no discontinuity in their scientific efforts.

Perhaps the depth of our feelings, as we pay homage, can be better conveyed through a story that took place in an age when men were matched against the towering force of elemental Nature.



Challenges of this sort could still be found at the turn of the century in the vast unexplored white-waste of Antarctica. As you read on, compare the magnificence of heroic deed to the eloquent, humble tribute that followed. In May, 1916, Sir Ernest Shackleton and his comrades Worsley and Crean had landed on South Georgia Island after crossing 700 miles of the most dreaded bit of ocean in the world, "Drake's Passage." These three men sailed from the "Screaming Sixties" to the "Raving Fifties" in a 22-foot open boat, so that they might rescue their marooned comrades. They had left them waiting hopefully on desolate Elephant Island, which had been reached after months of toil and hardship after the First Trans-Antarctic Expedition lost their ship, "Endurance", crushed in the ice pack of the Wedell Sea.

With wind velocity often gusting to 150-200 miles per hour, 80 foot waves traveling at 50 miles per hour, their frail craft was constantly threatened to sink under the weight of an iron-like sheet of ice formed as the hissing spindrift froze upon the improvised deck. Starved, ragged, exhausted, they reached land at a point where civilization was still twenty-nine miles from their grasp. Their torturous path to rescue across South Georgia's saw-tooth mountains and glaciers followed a route never before or since traversed by man, because "it is impossible." Miraculously, the impossible was achieved. They staggered into the desolate Stromness whaling station.

That night a crude reception was held for these three. In a large, smoke-filled room with the smell of rotting whale carcasses in the air, crowded captains and mates. Four white-haired veteran Norwegian skippers came forward. Their spokesman said that they had sailed the Antarctic seas for 40 years and that they wanted to shake the hands of the men who could bring an open 22-foot boat from Elephant Island through the Drake Passage to South Georgia.

"Then every man in that room stood up, and the four old skippers took Shackleton and Worsley and Crean by the hand and congratulated them on what they had done. There was no air of formality, no speeches. They had no medals or decorations to bestow—only their heartfelt admiration for an accomplishment which perhaps only they would ever fully appreciate. And their sincerity lent to the scene a simple but profoundly moving solemnity." (*From "Endurance" by Alfred Lansing*).

With this profound spirit of appreciation, understanding, and gratitude for their labors, the Cancer Issue of CONNECTICUT MEDICINE is dedicated to Drs.

Ottenheimer, Kendall, and Bristol. The example of their lives has enriched the three avenues through which medicine should be expressed: as a science, an art and a ministry. These pioneers for the cause of cancer control in this state, as founders of the Connecticut Division, left an indelible imprint of vitality and vision for now and all time.

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"Those who have learned from a great master must surely not be content to imitate his methods, but rather must strive to capture his authentic spirit, and in that spirit to seek for new roads, and so to discover still firmer truths. Few virtues are nobler than loyalty to a great tradition. But such tradition is kept alive not by routine observance of ancient ceremony, nor by mute obedience to outworn creed, but by active faith for ever seeking new truths and exploring new paths, in conformity with the old spirit, and with unfaltering devotion to that great ideal which tradition enshrines."

*Lord Moynihan, Abridged (1865-1936)*

EDWARD J. OTTENHEIMER, M.D. 1898-1963

Past President, New England Cancer Society  
Incorporator—Connecticut Division

- 1947-48 Member, Connecticut Division, Executive Committee
- 1948-49 Member, Medical Advisory Committee and Trustee
- 1949-55 Chairman, Medical Advisory Committee and Trustee
- 1953-55 Vice-President, Connecticut Division
- 1956-57 President of Connecticut Division
- 1951-61 Cancer Coordinating Committee of Connecticut State Medical Society
- 1960-63 Honorary Trustee

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"It becomes every man who purposes to give himself to the care of others, seriously to consider the four following things: First, that he must one day give an account to the Supreme Judge of all the lives entrusted to his care. Secondly, that all his skill, and knowledge, and energy, as they have been given him by God, so they should be exercised for His glory and the good of mankind, and not for mere gain or ambition. Thirdly, and not more beautifully than truly, let him reflect that he has undertaken the care of no mean creature, for in order that we may estimate the value, the greatness of the human race, the only begotten son of God became himself a man, and thus ennobled it with His divine dignity, and, far more than this, died to

redeem it. And, fourthly, that the doctor, being himself a mortal man, should be diligent and tender in relieving his suffering patients, inasmuch as he himself must one day be a like sufferer."

*Thomas Sydenham* (1624-1689)

RALPH E. KENDALL, M.D. (1895-1964)

Pathologist, Hartford Hospital

From 1940 An original Incorporator and Trustee of the Connecticut State Committee of American Society for the Control of Cancer: the antecedent organization of American Cancer Society, Connecticut Division. Leader in the organization of the Hartford Branch.

1946 Established first Cytology (Pap smear) Laboratory and Training Center in Connecticut under grant from Connecticut Division. This developed into one of the largest cytology services in the United States.

1953-55 Member of Medical Advisory Committee

1955-60 Chairman, Cytology Committee

1962 Awarded American Cancer Society Connecticut Bronze Award and Citation for Distinguished Service in the Field of Cancer

1951-55 Cancer Coordinating Committee of Connecticut State Medical Society

1960-62 Member, Executive Committee, Connecticut Division

1963 Honorary Trustee of Connecticut Division

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"Medicine, as I see it, is an art based on many sciences; the student, to be worthy of his art, needs ever to pursue knowledge and, even more, to have the spirit of knowledge. But in the application of his art to human needs, the doctor requires more than scientific knowledge; he needs, in addition,

insight, understanding, sympathy, and, perhaps beyond these the religion of helpfulness."

*Lord Dawson of Penn* (1864-1945)

DONALD A. BRISTOLL, M.D.

Obstetrician and Gynecologist, New Britain

From 1942 Incorporator and Trustee of the Connecticut State Committee of American Society for the Control of Cancer—antecedent organization of American Cancer Society, Connecticut Division. Leader in organization of New Britain Branch.

1945-57 President of New Britain Branch

1953-60 Member, A.C.S./Connecticut Division, Executive Committee

1956-60 Served as Professional Delegate to ACS, National Society.

1957-59 President, ACS Connecticut Division

1960 Awarded American Cancer Society Bronze Medal and Citation Award for distinguished Service in Cancer Control

1960-63 Honorary Trustee of Connecticut Division

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These men knew that man's great effectiveness lies in his example. The test of a man's real philosophy is his living of it. In this, there is not only strength of personal character, but also a type of existential truth that needs no other testing.

"So, take and use thy work,  
Amend what flaws may lurk,  
What strain o' the stuff, what  
warpings past the aim!  
My times be in thy hand!  
Perfect the cup as planned!  
Let age approve of youth, and  
death complete the same."

*Robert Browning*

(final stanza, *Rabbi Ben Ezra*)

HENRY M. WILLIAMS, M.D. *Guest Editor*



# A Universal Responsibility

Henry M. Williams, M.D., Guest Editor

■ Remarkably, the basic orientation of cancer therapy has undergone profound alteration in recent years without comment or even recognition. Modern concepts now require that therapy, whether new or old, be applied clinically through a well-coordinated, multidisciplinary approach to cancer management. Lest you harbor suspicions that this does not truly mark a change, remember that but a scant decade ago, responsibility for the full range of clinical neoplasia was shouldered alone by surgeons and radiotherapists.

Although the combined efforts of a variety of disciplines promises much, it is at the same time disquieting to discern a gap between current salvage rate for accessible cancer and those possible by application of the most basic techniques of cancer diagnosis and treatment. The proportions of this "application-gap" can be apprehended only by a critical analysis of failure, that both shuns the bias of remembered individual success and resists the surrender of personal responsibility to technology. A system of medicine responsive to change and success can mature only after hours of reflective despair and should be practiced with the delicate hand of restraint.

The clinical course of unsuccessfully treated cancer assumes a new dimension when related at each phase to the peaks of professional interest and activity normally stimulated. Two peaks may be depicted graphically, one at the time of initial diagnosis and therapy, the other with clinical recognition of metastatic disease. Interpreted broadly, the voids between may be paraphrased: 1. events before initial diagnosis and treatment (*cancer detection*); 2. the lag phase between initial therapy and clinical recognition of metastatic disease (*reappraisal of initial therapy*); 3. the period of ongoing management of active metastatic cancer subsequent to initial palliative efforts (*quality of survival*). While admittedly arbitrary, the three areas not only indicate the reasons for the application-gap, but also point out a variety of near-unexploited approaches to cancer control.

## 1. Cancer detection

Regretably, the piecemeal process of education tends to sequestered knowledge from wisdom. Is it possible that, by repeated emphasis, the basic techniques of early detection of accessible cancer have become isolated from the ordinary demands of

meticulous medical practice? If so, it would give comfort to those who insist that it is impossible to provide a vital part of proper medical supervision to a wide population. More specifically, it would detract from the necessity of an annual comprehensive history and physical examination, which includes pelvic examination and pap smear, digital rectal and sigmoidoscopic examination, routine chest film, hemogram, urinalysis and chemical test for occult intestinal bleeding.

## 2. Reappraisal of initial therapy

Continuous reappraisal and justification of specific therapy is a moral obligation inseparable from the other demands of clinical medicine. Although periodic collective review of techniques and results may satisfy statistical criteria, the essential ingredient of acceptable medical and surgical practice remains "individualization of therapy". "Routine management" of any clinical problem, neoplastic or otherwise, invites a brand of automatic medical thinking inextricably linked to the mediocre.

These issues are not always easy to settle. For example, to insist that radical mastectomy is always justified for operable breast cancer becomes ever more difficult to defend. The variable biologic potential of carcinoma of the breast demands a more flexible philosophy that includes individual application of one of several effective therapeutic schemes. Among the obstacles to a well-ordered study of this problem is the difficulty any practitioner experiences reconciling what he feels is best for one patient to a rigid protocol employing randomized selection of therapy. Hopefully, through periodic reappraisal of results, criteria of selection for radical curative therapy may become so refined, as to virtually eliminate the tragedy of unsuccessful therapy.

Selection of patients for palliative therapy should also be done with as much forethought and care as used for curative procedures. The importance of formulating proper criteria is nowhere more apparent than in the relatively unselective way in which Stage 2 and Stage 3 ovarian carcinomas receive radical abdominal-pelvic irradiation. The early relapse rate in anaplastic ovarian cancer, in

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DR. HENRY M. WILLIAMS, Associate Attending Physician, Hartford Hospital, Hartford, Conn.

particular, as well as other Stage 3 patients following extended irradiation, argues for the introduction of a new approach. Possibly the use of (enlightened) chemotherapy initially might at one and the same time improve results and reduce morbidity.

Advances in radiation therapy and chemotherapy have introduced two new issues related to therapeutic philosophy. First, criteria for operability may well change or at least require modification should either or both of these modalities effectively convert clinically inoperable cancer to potentially resectable disease. Concurrently, as the immunosuppressive effect of extensive exposure to ionizing irradiation or the ability of antineoplastic chemicals to paralyze the immune defenses of the host become more evident, a totally new approach to cancer chemotherapy may be necessary. A major influence in developing modified (less vigorous) dose schedules has been the fear that the value of these agents could be offset by creating an immunoincompetent host, susceptible perhaps, not just to infection but also to the unrestrained (by antibodies) proliferation of tumor cells.

### 3. *Quality of survival*

Realizing that every effective form of cancer therapy imposes the risk of treatment-associated morbidity to some degree, the concept of quality of survival arose in an effort to reconcile these opposing influences. Here too, there is no right or wrong; rather, probability in the last analysis holds sway. An abdominalperineal resection for rectal cancer that fails to provide even one year's survival is both quantitatively and qualitatively unrewarding. But if the discomfort associated with untreated or even inadequately treated disease exceeds the morbidity of abdominoperineal resection, we can hardly term the procedure unrewarding. Further, our responsibility to provide maximum opportunity for cure or excellent palliation, if discharged properly, imposes upon an irreducible minimum the risk of unsuccessful therapy which may also engender qualitatively undesirable morbidity.

During the ongoing phase of management of metastatic cancer, quality of survival provides a most useful goal. Since therapeutic decisions at this stage do not involve curability, therapeutic morbidity becomes a matter of even deeper concern.

Quality of survival may be further refined by altering the quantity of therapy; quite surprisingly, we find that without necessarily compromising results toxicity can be sharply curtailed. Actually, concern for the qualitative aspects of survival stimulated development of a new chemotherapeutic philosophy, employing combinations, sequences and alternating patterns of drug administration. By so doing, individual drug doses may be reduced with associated improvement in therapeutic index.

Quality of survival means much more than mitigation of surgical failure or drug toxicity. It conveys the essential medical expression of humanitarian concern for total patient welfare: preservation of individual dignity, freedom from fear of the unknown, elimination of unnecessary mental obtundation, prolongation of enjoyable productivity with an associated shorter "terminal phase".

We must also remember that hope and truth are not mutually exclusive terms. To take away hope in an exaggerated show of "honesty" is to take away life itself. Truthfully, something constructive can always be done for a patient, no matter how dire the medical circumstances. Specific antitumor therapy quite often brings unexpected additional benefits not necessarily dependent upon objective regression of disease, such as pain relief or an improved sense of well being. Conversely, symptom-relief in cancer does not always require administration of specific antineoplastic agents. Only the bounds of ingenuity limit the number and variety of helpful ways open to every physician who would alleviate suffering.

If nothing else, a closer look at the three areas of diminished clinical activity establishes beyond question the premise that clinical problems associated with cancer are not unique; the basic tenets of medicine apply and should be applied. An orderly, logical approach to diagnosis of both the patient's ailment and what ails the patient usually suggests proper therapy. For as long as rejustification of treatment remains an ingrained habit, there is little danger of straying far from the ultimate commitment of medicine: preservation or restoration of that joyous equilibrium with nature we are pleased to call "health", while providing continuous support of individual identity and human dignity.



# Carcinoma Of The Female Breast: Current Thoughts

Ira S. Goldenberg, M.D.

## Early Breast Cancer

*Surgical Treatment.* Halsted stated with assurance in 1895 that "... cancer of the breast is a curable disease if operated upon properly and in time." He described the surgical approach to breast cancer which has remained, until recently, the generally accepted therapeutic modality. During the past decade, however, many thoughtful physicians have questioned whether radical mastectomy is, in fact, the best therapy. These queries have been based on the obvious failure of the operation to cure many women. Studies by Shimkin<sup>14</sup> and Kaae and Johansen,<sup>10</sup> to cite only two reports, have suggested that simple mastectomy, a lesser surgical procedure than removal of the breast in continuity with the pectoralis muscles and axillary lymph nodes, may be consistent with survival patterns analogous to those of radical mastectomy. Simple mastectomy may be associated with fewer psychological and physical problems<sup>7</sup> than the radical operation and it is reasonable, then, to perform an operation which presents fewer post-operative complications if, indeed, survival is not altered.

Simple mastectomy followed by radiation therapy delivered to the chest wall and regional lymph nodes has been advocated by McWhirter though it should be emphasized that the method of application may determine success or failure with this modality. Various sources of ionizing radiation and different therapeutic fields have been employed in years past, but the McWhirter megavoltage technique,<sup>11</sup> which incorporates tangential chest wall areas (to include internal mammary lymph nodes as well as the chest wall itself) and "shoulder fields" (to include other regional nodes, i.e., axillary, supraclavicular and posterior cervical) seems best at the present time.

Unfortunately, there have been few reports<sup>2,10</sup> of randomized studies to evaluate the efficacy of radical mastectomy as compared with less radical procedures, with or without added radiation therapy. Such studies are currently in progress in several centers and will eventually offer more complete statistical evaluation as to how each procedure may affect patient survival patterns. Until that time, differences between these treatment plans must be appraised by the individual physician as he decides which primary therapy of breast cancer should be utilized in a given patient.

This decision is even more difficult to make in view of recent reports of widely varying approaches to the problem. At one extreme, Crile<sup>4</sup> has recently

related his experience with simple excision of the cancer, and in selected patients, longevity did not differ significantly from that for other forms of treatment. Such therapy must undergo further evaluation, however, before it can be considered more than a therapeutic curiosity. As opposed to this, there are advocates of very extreme surgical procedures. The supraradical mastectomies described by Urban<sup>15</sup> and Dahl-Iverson,<sup>6</sup> however, have not been demonstrated to be more effective in prolonging the cancer-free interval and survival than other procedures and there appears to be no proven place for them despite theoretically sound design.

*Postoperative Cytotoxin Administration.* Although the mechanism of establishment of metastatic foci is unknown, it has been suggested that tumor cells may break off during operative manipulation, enter the circulation and be carried to distant sites, thus establishing metastases. This possibility has led to the concept that intravenous administration of cytotoxic agents during and immediately after operation might perhaps act prophylactically to kill these circulating cancer cells before they establish frank metastases. A controlled study based on this thesis was started several years ago under the sponsorship of the U.S. Public Health Service using triethylenethiophosphoramide at varying dosage levels after radical mastectomy. Preliminary results, which were widely publicized in the lay press, indicated that the cancer-free interval and patient survival were prolonged in the test group of patients to whom the cytotoxic agent was given as compared to a control group which received a placebo. Since that time, a more extensive report has been prepared which indicates little significant difference between the control and the test group and which, unfortunately, has received little attention from either the professional or lay press. It seems apparent that these agents which destroy cancer cells may also be harmful to normal cells and alterations induced in the patient may be extensive and even fatal. Such therapy needs further controlled investigation before it can be accepted as valuable to the patient with early breast cancer.

*Castration.* And what is the role of castration in the woman with breast cancer? This is a point of

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DR. IRA S. GOLDENBERG, Associate Professor of Surgery, Yale University School of Medicine, New Haven, Conn.

much thoughtful discussion at present and as yet no definite conclusion can be reached, although a great deal of suggestive evidence has been gathered both retrospectively and prospectively. It appears that some women with breast cancer are adversely affected by the presence of ovarian estrogen secretion. Elimination of the influence by surgical or radiation castration (of equal effectiveness) brings about regression of metastatic foci in women with so-called "hormone dependent" cancer (about one-third of the total). Many physicians have felt that castration is indicated only when metastases have developed and in this way "hormone dependence" could be ascertained and a potent weapon against the disease be unleashed simultaneously. Others have felt that castration should be performed early in the course of the primary disease, perhaps "prophylactically" to avoid the development of metastases. The latter view requires an extensive randomized trial for proof although Nissen-Meyer<sup>12</sup> recently completed a randomized study, elaborating on a preliminary report, which indicates that the cancer-free interval may be prolonged in women who have been castrated early, although survival may be little affected. He also found that naturally menopausal women, to the age of 70 years, have significant ovarian estrogenic production and radiation "castration" of these patients may also be advantageous to control metastatic breast cancer and prolong life.

### **Advanced Breast Cancer**

*Radiation Therapy.* There can be little doubt that assiduous treatment of women with advanced breast cancer pays dividends in comfort as well as increased longevity for the afflicted patient. Radiation therapy and hormonal alterations are presently the mainstays of such therapy. Limited palliative radiation can relieve metastatic bone pain dramatically, reduce the size of cutaneous or lymph node masses and improve hepatic and cerebral symptomatology. Orthovoltage therapy is often adequate and can usually be administered in a single treatment session, especially to bone lesions. The development of megavoltage therapy has opened a new era of palliation for visceral lesions, formerly unapproachable with ease and safety with orthovoltage, which can now be treated with excellent palliative results in many patients.

*Hormonal Alterations.* Much confusion still prevails as to the precise role of hormonal therapy in the woman with breast cancer. Castration as a modality of therapy has already been discussed and comments here will be restricted to exogenous hormone administration, adrenalectomy and hypophysectomy.

The mechanism of hormonal action at the level of the cancer cell metabolism is unclear. It has been

suggested that degradation of androgens to estrogen explains how male hormones work and this suggestion has been corroborated by the demonstration of elevated urinary estrone in women receiving testosterone propionate,<sup>13</sup> one of the most effective androgenic agents. Other androgens, however, which also produce objective remission of metastases do not cause this elevation of urinary estrogenic degradation products. As was pointed out earlier, removal of endogenous ovarian estrogens is beneficial in some women, but so also is exogenous estrogenic therapy. Perhaps an answer to this seeming enigma is dosage: a certain level of female hormone may inhibit, while another promotes, tumor growth. This finding has been noted in experimental animal tumors.

The primary choice of an exogenous hormone for treatment of metastatic breast cancer is not clearly defined at this time. Some experts advocate androgenic preparations while others feel that estrogens are preferable. In years past it has been common practice to administer estrogenic substances to the older woman with soft tissue lesions and reserve androgens for patients with bone involvement. A recent study, however, indicated that testosterone propionate can cause objective remissions most effectively in women with breast, node or skin metastases who are more than five years menopausal.<sup>8</sup> Data from this same study leads to the inexorable conclusion that androgenic therapy can produce objective remissions in all age groups and all sites of lesions. Virilization is almost always a problem, however, with testosterone propionate. Estrogens seem to have their greatest application in women who object to the induction of unpleasant androgenic effects or patients in whom primary male hormones fail to control the disease. It should also be appreciated that subjective improvement may follow administration of hormones and such a result alone can justify the unpleasant physiological effects that might be induced.

Natural hormone secretions in the individual patient are complex and not yet completely measurable in the laboratory, while the interaction of endogenous with exogenous hormones is also unclear. Thus, at the present time, additive hormonal therapy should be utilized only in menopausal or castrated patients for maximum effectiveness.

A program is being conducted by the Cancer Chemotherapy National Service Center, U.S. Public Health Service, and many cooperating institutions, to develop new hormonal agents which are potent against cancer but devoid of undesirable physiological effects. Several hormones emanating from this program have already demonstrated clinical merit.



Great masses of data have been gathered regarding the effectiveness of adrenalectomy and hypophysectomy in the therapy of advanced breast cancer. Surgical removal of adrenal estrogenic production is rational in the absence of ovarian function (natural menopause, radiation castration, or preferably, oophorectomy) and objective remission of metastases may occur in about one-third of women so treated. Replacement therapy is accomplished with ease at this time and adrenal insufficiency problems are of no concern.

Ablation of pituitary function also allows metastases in about 30 per cent of such patients to remit objectively. Surgical excision of the gland has been the preferred approach for many years, but recent investigation confirms the effectiveness of megavoltage radiation techniques. Lack of adrenocorticotrophic hormone production with subsequent decrease in adrenal estrogenic hormone production may explain why hypophysectomy is effective, but some suggestions have been made that removal of pituitary growth hormone or other similar fractions may be important also in aiding metastatic regression.

I feel that adrenalectomy and/or hypophysectomy should be reserved for those patients who have previously demonstrated remission after castration or exogenous hormone administration and who again have progressive disease. Such stepwise therapy may allow a prolonged survival. These procedures are not something for the occasional surgeon to perform and even in the most skilled hands morbidity and mortality may be considerable.

It should also be pointed out that mere suppression of endogenous adrenal hormone production by the administration of exogenous adrenal steroids, a "medical adrenalectomy", may induce remission of metastases. This view has been championed by Nissen-Meyer<sup>13</sup> who believes that as little as ten milligrams of prednisone daily may be effective.

**Cytotoxins.** Cytotoxic agents have been used also in the treatment of advanced breast cancer, but results have been poor with the variety of agents evaluated to date. Hormonal alteration is still the most effective way to treat this disease and the use of cytotoxins must remain an experimental modality until more conclusive benefits are demonstrated.

### Some New Concepts

**Hormonal Milieu.** Recognizing the probably important role of the hormonal milieu of women with breast cancer, several investigators have attempted to evaluate whether natural endocrine differences may exist among patients which might be related to the course of the disease. Bulbrook et al<sup>3</sup> noted that

women who did not respond to the ablative techniques of adrenalectomy or hypophysectomy as therapy for advanced metastatic disease had abnormally low amounts of etiocholanolone in their urine. This androgenic derivative seemed to occur in normal amounts in women who demonstrated objective improvement of metastatic lesions after ablative hormonal operations. Further evaluation of urinary adrenocortical products revealed a relationship between 17-hydroxy corticosteroids and etiocholanolone. A "discriminant" was developed retrospectively depicting this relationship which could be expressed in *negative* terms for *non-responders* to ablative techniques and *positive* terms for *responders*. The predictive value of this discriminant before operation was then demonstrated, and it has now further been shown that about half of women with early breast cancer also have negative discriminants.<sup>9</sup> This finding suggests that the subnormal androgen secretion in some patients may be associated with cancer development and growth. Perhaps the mechanism may be lack of antagonism to the normal amounts of estrogen which act as carcinogens for long periods of time on breast epithelium. These theories are being evaluated further by determination of the urinary hormone end products in a normal population of about 5,000 women between the ages of 35 and 55 on the Isle of Guernsey in Great Britain. Periodically collected 24-hour urine samples are being analyzed and correlation attempted between the calculated discriminants and the 3-4 per cent of this population sample who can be expected to develop breast cancer during the several decades of the study.

A ramification of this project has also been started in London, in which small amounts of androgen are administered to women with breast cancer after discriminant determination and mastectomy. A random control group is receiving no hormone supplement. If the theories are correct, some protection may be afforded those women receiving the androgen and they should have a better prognosis than the control group, especially if negative discriminants were present before mastectomy.

**Tumor-Host Interactions.** One of the great unknown quantities in human cancer etiology and pathogenesis is the possible role of immune reactions of host to tumor, infectious antigens usually causing a change in the host lymphoreticuloendothelial system. Immunological reactions of the hyperimmune type are associated with antibody formation while those of delayed bacterial hypersensitivity are commonly reflected in altered circulating lymphocytes without free antibodies. Alteration in axillary lymph node structure in women with breast cancer has been noted by Black.<sup>14</sup> In particular, an increase in the number of his-

tiocytes in the sinusoids has been found to marked degree in about one-fifth of patients. These changes have not been noted in nodes of patients without cancer or in patients with colon cancer, although many gastric cancer patients also show similar alterations. The degree of sinus histiocytosis can be measured and when correlated to known survival patterns,<sup>5</sup> it has been possible to demonstrate a linear relationship, i.e., those patients demonstrating a marked degree of sinus histiocytosis had the best survival experience.

Such evidence of an immune response is, at best, fragmentary, but it does give an indication of an area where further investigation is mandatory. It may not be too farfetched even to think of the possibility of enhancing any immune reactions which may be present with the hope of increasing longevity.

### Summary

It has been the purpose of this article to present and discuss the modern, multidisciplinary management of female breast cancer. It should be eminently clear from the foregoing that there is no generally agreed "best" management of the patient. Time-honored concepts are being toppled at a rapid rate and doubt is rampant that any but a few breast cancer patients are curable at all. This is not to say that the physician is defeated in his quest for cure, but it is now obvious that he traverses vast unknown and contrary areas of medical thought as he tries to decide what to do for his patient. It is my opinion that radical mastectomy is doomed as primary surgical therapy for this disease since to date it has not proven superior to less extreme and less psychologically disturbing procedures. Post-simple mastectomy radiation therapy, according to the technique of McWhirter, seems to offer something more than operation alone, and should be used. Castration early in the course of the disease, although not conclusively proven to benefit every woman, should be performed in all premenopausal patients (and probably in postmenopausal women to the age of 70) recognizing that the possible physiological and psychological problems of artificial menopause are lesser evils than the possibilities of shortened cancer-free interval or survival time. Radiation castration properly performed is as effective as ovarian excision.

If metastases appear, radiation therapy should be employed promptly when it can be reasonably expected to be effective, either alone or in combination with hormone administration. Androgens are probably more efficacious than estrogens in the majority of women when progressive metastatic disease is present and the search for new hormones may ultimately produce a non-toxic preparation without desirable physiological effects.

Chemotherapy with non-hormonal agents in the early phase of the disease is still experimental and is a last resort in patients with advanced disease. And finally, adrenalectomy and hypophysectomy should be considered severe treatment for severe disease, and may be employed when a reasonable hope exists for improvement after the operation.

This is where we are to-day. New developments continue to alter opinions and necessitate an open mind to progressive innovation. Hopefully, the future may bring us clearer definitions of optimum therapy.

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# Cancer Of The Colon And Rectum

Harry J. Tamoney, Jr., M.D.

## Introduction

■ With the exception of cancer of the skin, cancers of the colon and rectum are the most common in the United States. The American Cancer Society reports a death rate from these lesions of 42,900 for the year of 1964.<sup>1</sup> Deaths from lung cancer that year were 47,000.<sup>1</sup> The discrepancy here is readily understood when we realize that the incidence of cancer is not absolutely reflected in the death rate. Although nowhere near optimum, the survival rate of patients with colorectal cancer is so much higher than that for those with lung cancer that the annual death rate is lower. Another interesting comparison is that with gastric cancer. Ten years ago the incidence of gastric neoplasm matched that in the colon and rectum. Since then, for reasons which are not clear, there has been a sharp decline in the incidence of gastric cancer. We can hope that colorectal cancer will follow this pattern of declining incidence, but until then our goal remains early diagnosis and treatment.

It is discouraging to note in 1965 the still large percentage of patients who arrive for treatment in a late stage of this disease. While the statement that the fate of the patient with cancer of the colon and rectum is the responsibility of the first physician consulted is still at least partially valid, numerous other opportunities are present today. Teams of the various disciplines of medicine are now available in most of our communities and their efforts should increase the survival rate in this disease. The effect of this effort has been most noticeable in the drop in operative mortality rate from 25 per cent to today's 3-4 per cent.<sup>2</sup> However, a similar decrease has not been found in the five year survival rate from this cancer. If the team concept could be applied to the problem of earlier diagnosis an improved survival rate might be expected.

It is the purpose of this article to explore some of the areas pertinent to colorectal cancer and to review recent contributions.

## Symptoms And Diagnosis

Many authors divide cancer of the large bowel into the three divisions, right colon, left colon, and rectum when they discuss symptoms. Differences in anatomy and function cause early cancers in these geographic areas to present differently. These are depicted in Figure I.

FIGURE I  
SYMPTOMS OF COLON AND RECTAL CANCER

|                        | RIGHT COLON                                         | LEFT COLON                                                                                          | RECTUM                                                                      |
|------------------------|-----------------------------------------------------|-----------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------|
| 1. Lumen               | Large—not liable to cause obstruction               | Small—obstruction                                                                                   | Large — obstruction infrequent                                              |
| 2. Feces               | Liquid                                              | Solid                                                                                               | Solid                                                                       |
| 3. Peristalsis         | Good                                                | Slow                                                                                                | Good                                                                        |
| 4. Function            | Nutritional absorption                              | Storage                                                                                             | Expulsion                                                                   |
| 5. Bleeding from tumor | Not grossly                                         | Blood on stool grossly                                                                              | Bleeding grossly or blood on stool                                          |
| 6. Chief Complaint     | Nonspecific                                         | Related to bowel habits                                                                             | Related to expulsion                                                        |
| 7. Symptoms and Signs  | 1. Abdominal pain<br>2. Anemia<br>3. Abdominal mass | 1. Alternating constipation and diarrhea<br>2. Blood on stool<br>3. Obstruction<br>4. Size of stool | 1. Bleeding<br>2. Tenesmus<br>3. Incomplete evacuation<br>4. Mucus diarrhea |

Attention to early symptoms should lead to diagnosis in time for successful therapy. Repeated X-ray studies are warranted, especially when right sided lesions are suspected, since tumors of the cecum and right colon are the most difficult to visualize. This is understandable as the cecum and ascending colon are often difficult to fill with barium, and a good mucosal pattern may not be obtained. In addition, the patient is occasionally uncomfortable at this stage of a barium enema examination and, thus, inclined to be uncooperative.

It should be remembered also that the stage of the disease as well as the virulence of the tumor will influence the symptoms. Progression into the acute problems of obstruction, perforation, and hemorrhage is possible at any time.

While it is unfortunately true that a few patients will develop cancers that are silent until an incurable stage has been reached, over 95 per cent of the patients could be diagnosed at an early and potentially curable stage.

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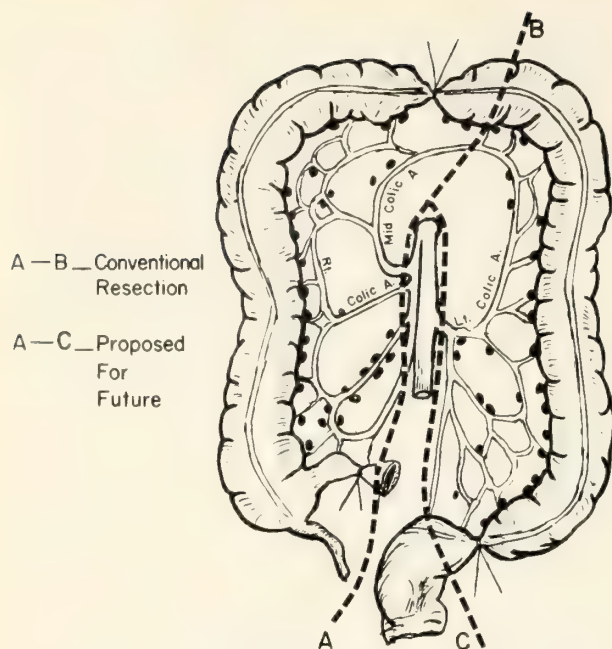


FIGURE II

Plan for the extension of surgery for tumors of the cecum and right colon in patients less than 55 years old.

### Treatment

#### SPONTANEOUS REGRESSION

In 1959 Everson and Cole<sup>3</sup> presented 112 cases of documented instances of spontaneous regression of cancer collected from the literature since 1900, and, recently Rankin<sup>4</sup> reported the case of a 44 year old white male whose liver metastases from a rectal cancer disappeared. These metastatic liver lesions had been biopsied during an abdominal perineal resection for his primary cancer. At laparotomy, ten years later for treatment of a second primary, cecal carcinoma, the liver metastases were gone. These reports suggest two considerations.

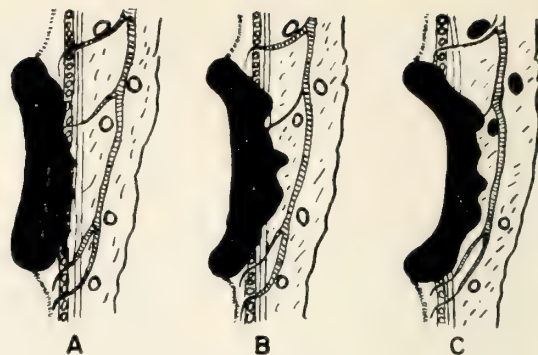
1. Palliative resection of colonic or rectal cancer in the presence of liver metastases is justified.

2. The incidence of multiple bowel primaries adds weight to the proposal of subtotal colectomy for primary colon cancer in patients less than fifty-five years old. (Figure II)

#### SURGERY — CURATIVE

Surgical extirpation of colorectal cancer, although often inadequate, still offers the patient his best chance of cure. Many refinements beyond simple resection of the tumor have come about, and increased knowledge of the route of spread of the cancer and its biological behavior has stimulated the use of new and more extensive resections. Improvements in anesthesia, blood replacement, and antibiotics have permitted these procedures to be carried out with safety.

When the tumor is localized to the bowel mucosa (Dukes A) (Figure III) 95 per cent of patients will



- A -- Growth limited to wall of rectum.  
 B -- Extension of growth to extra-rectal tissues but no metastases in regional lymph nodes.  
 C -- Metastases in regional lymph nodes.

FIGURE III

Duke's original classification of bowel cancer.

be completely cured by simple extirpation or segmental bowel resection. The problem, however, is in diagnosing this stage in the gross. Inasmuch as this problem has not yet been solved, we must depend on our knowledge of how cancer spreads in developing proper therapy.

There are four possible routes by which cancer cells may leave their primary site in the bowel:

- 1) By contiguity
- 2) By implantation
- 3) By vascular spread
- 4) By lymphatic spread

Vascular spread fortunately is late and does not usually occur until the lymph nodes have been involved. Vascular spread carries the worst prognosis. Sunderland<sup>5</sup> reported a 5 year survival of 57 per cent in patients who had lymph node involvement from colorectal cancer compared to 20 per cent survival rate of patients who had venous invasion. The significance of this is further illustrated by Grinnel<sup>6</sup> who reports a 5 year survival rate of 75 percent without venous invasion compared to 37 per cent in patients with vascular spread.

It is in this area that adjunctive chemotherapy may well play an important role. Thio-Tepa, Nitrogen Mustard, and other cancericidal agents are presently being employed. These drugs are being given systemically, as well as regionally during the surgical procedure. (Figure IV) They may be of assistance to those patients with late cancer who already have early vascular spread, but more likely their value will lie in the control of tumor cell emboli liberated by manipulations involved in the surgical resection<sup>7, 8, 9</sup>

The development of a recurrence at the anastomosis following resection for cancer of the colon has been studied by Cole and others<sup>10</sup> for over ten years. They have proved that implantation at the



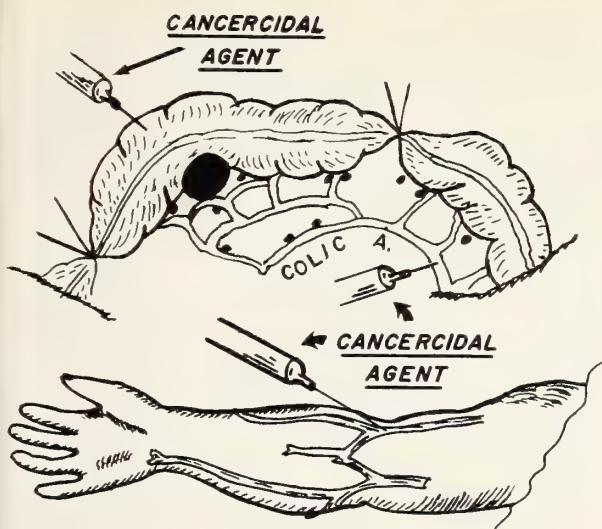


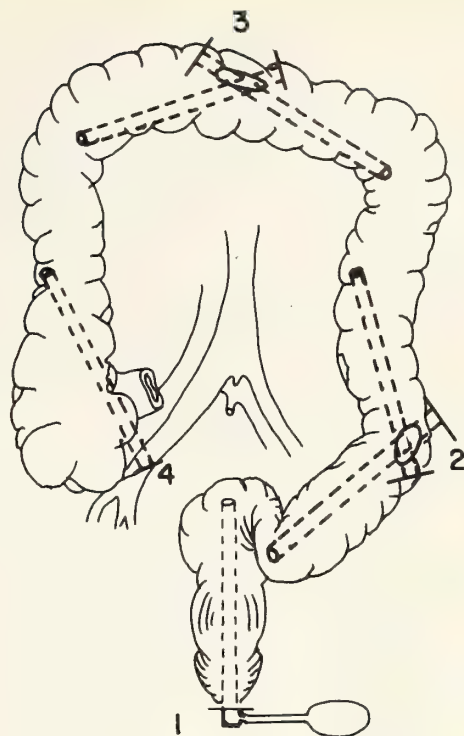
FIGURE IV

Agent instilled into segment of bowel containing the cancer, or to its blood supply or systemically to entire body should at least lower the number of possible circulating cancer cells.

time of surgery can occur and by ligation of the bowel several centimeters above and below the tumor mass early in the operation, as well as irrigation of the bowel lumen prior to anastomosis, they have almost completely eliminated local recurrences. The use of iodized catgut<sup>11</sup> may further decrease the incidence of tumor implantation at the anastomotic area.

Surgical procedures for resection of colorectal tumors have gradually become standardized with simple segmental resection being replaced by right or left hemicolectomy or subtotal colectomy, as well as abdominal-perineal resection. Better knowledge of the pathways of lymphatic spread has provided the impetus for the more radical extensive operations. Initial ligations of the blood vessels supplying the segment of cancerous bowel at aortic and portal levels as well as base of mesentery excisions encompassing the lymphatic drainage in its entirety determine how much bowel need be sacrificed.

In addition to this primary surgery directed to the bowel, knowledge of alternate methods of spread has prompted accessory excisional procedures. Since there is a reported 8 to 12 per cent incidence of metastases to the ovaries in a Krukenberg fashion, bilateral oophorectomy should now become a standard part of the primary operation. Madden,<sup>12</sup> moreover, has demonstrated that inclusion of the spleen and tail of the pancreas may well increase the salvage rate of transverse and splenic flexure lesions since lymph drainage has been identified in this direction as well as along the customary mesenteric pathways.



## TECHNIQUE & SEQUENCE OF EXAMINATION

FIGURE V

Steps 2-3-4 should be routine when laparotomy for removal of an intra-abdominal polyp is warranted. The finding of additional unknown pathology by colonoscopy is not infrequent.

Brunschwig's exploration<sup>13</sup> of the possibility of subtotal or segmental hepatic resection for metastatic deposits is interesting. If the solitary embolic phenomena theory of metastases is correct this approach may prove rewarding.

In the instance of late locally advanced lesions with no distant spread, cure is possible through a multiorgan resection such as pelvic exenteration. If these patients are very carefully selected, a gratifying, though small, salvage will be effected.

### THE SECOND LOOK OPERATION

An aggressive approach to improving the survival rate of abdominal cancer was initiated by Wangenstein in 1948. He felt that unrecognized residual cancer left after primary colonic resection could be completely extirpated months later. He embarked on a program of re-exploring patients who had positive lymph nodes at initial operation, but who on followup later were asymptomatic and had negative X-ray studies. If residual cancer was found and removable, he continued these explorations at 6-12 month intervals until he either found no disease or non-resectable cancer.

At first approximately 50 per cent were found to have residual cancer. This has declined to 25 per cent in the past two years,<sup>14</sup> since such modifications

in the primary operation as pericaval and periaortic lymph node dissection have been adopted. Thus, while the need for the *Second Look Procedure* is now less, we are indebted to Dr. Wangenstein for his approach which was most beneficial in delineating the pathways of early spread of colon cancer, and led to a more proper and adequately designed primary operation.

#### **PALLIATIVE SURGERY**

The common adage of "open and close" should be discarded by the surgeon who finds non-resectable disease at operation. Rather, he should focus upon the possibilities of preventing some of the unpleasant and painful complications which might arise in the patient's remaining life time. If the primary tumor can be safely removed, this should be done, in spite of the presence of liver metastases or other accepted signs of incurability. Removal of the omentum will reduce the amount of future ascites. The rectus wick operation is similarly useful in this connection. Removal of the ovaries will prevent the development of a Krukenberg type tumor. A prophylactic colostomy is preferable to a later emergency procedure. An intestinal bypass procedure may also be foresighted.

The use of secondary surgery should not be overlooked in the management of primary operative failures. One is tempted to think only in terms of X-ray therapy, chemotherapy or symptomatic pain relieving drugs when encountering this problem. Re-resection at the primary site of the lesion has been accomplished with increasing success in the author's experience, especially in the instance of anastomotic recurrences. An abdominal-perineal resection can at times accomplish what a previous low lying anterior resection failed to do, although a multi-organ resection may be necessary. While recent advances such as liver scans for metastatic disease have lessened the use of exploratory laparotomy as a diagnostic tool for determining whether local or disseminated disease is present, it still has a place. In the symptomatic patient its role is clear. When unexplained gastrointestinal symptoms appear following therapy for cancer of the bowel, a diagnostic laparotomy should be performed in spite of negative X-ray and other investigatory tests. Even if extirpation of the tumor encountered is not possible some of the other procedures mentioned above may be of benefit.

#### **X-Ray Treatment**

While X-ray therapy offers little as a definite modality, recent studies of preoperative irradiation of rectal cancer have been encouraging. Stearns<sup>15</sup> feels that it inhibits the dissemination of cancer cells at time of surgery and their ability to implant and grow. Patients with cancer of the rectum were

given 1200 to 1600 r preoperatively, and an improved 5 year survival rate was convincingly shown in those patients with lymph node metastases (Dukes C). Nakayama<sup>16</sup> has confirmed these studies of preoperative irradiation and Deddish<sup>17</sup> and Kleigerman<sup>18</sup> found no increase in morbidity from its use.

The fact that neoplastic tissues are frequently deficient in oxygen because of a poor blood supply relative to the bulk of the tumor, or because of its abnormal growth pattern, has led some investigators to add a high pressure oxygen technique to the usual radiation procedure. They feel that the higher the concentration of oxygen in and around the cancer cell, the more susceptible it will be to radiation therapy.

Another interesting approach to increasing the value of irradiation is the use of ceramic microspheres.<sup>19,20</sup> This method is designed to give a high concentration of a cancericidal agent such as Yttrium<sup>90</sup> to the tumor area without adverse effects on the body as a whole. Up to 100,000 rods can be given a local area with this method.

X-ray therapy does play an important palliative role. It is especially effective in ameliorating the crippling pain of bony metastatic disease.

#### **Chemotherapy**

The surgical and X-ray treatment methods of cancer of the colon and rectum have become increasingly more delineated to a point where further refinement or advance is unlikely and progress appears to be at a standstill. Their limitations have become well established and yet it is universally accepted that the mortality rate for this disease is far higher than desirable. It is only to be expected then that any new or different type of therapy would receive avid enthusiasm and rapid exploitation. This has been especially true with the introduction of chemotherapy where a whole new horizon is present.

Chemotherapeutic or anticancer agents can be administered to the cancer patient regionally to the area of tumor by perfusion or infusion techniques or systemically to the whole body. Perfusion is short term circulation of an agent through an anatomic site entering by an artery and leaving by a vein. This is mechanically controlled and requires an extracorporeal circuit. A temporary isolation of the area is created allowing the drug to come directly in contact with the tumor at a dosage which would be prohibitive otherwise. Eight to ten times the maximum systemic dose of the anticancer drug can be given with this technique.

Arterial infusion is an alternate method of regional therapy where a cancericidal agent is directed into the specific arterial blood supply of the tumor



site without isolation or attempt to prevent its entering the systemic circulation. This is performed continuously to the tumor in doses that the entire body can tolerate.

Neither of these two methods of chemotherapy has as yet been of any benefit to patients afflicted with colon and rectal cancer.

The use of chemotherapeutic agents systemically has been the method of choice with gastrointestinal tumors. Many alkylating agents as well as anti-metabolites have been used with varying results. 5 Fluorouracil, an antimetabolite, has been the most popular and certain documented periods of good palliation have been noted. Its role has not yet been fully evaluated. Until more information is gathered the use of such drugs remains experimental. Complete explanation to, and acceptance by, the patient, who must possess full knowledge of toxicity and side reactions, is mandatory before such therapy is undertaken.

I feel that, until a better drug is developed, 5 Fluorouracil should be offered to the patient for whom all other methods of therapy are useless. This, however, should be done at a time before he becomes critically ill or terminal. I have seen a few patients' lives extended three to eight months—and these have been months of symptom free living.

**The Treatment Of Polyps**

The concept that polyps of the rectum and colon are precancerous has been discussed previously, but their management is worthy of further comment. Fortunately, most of the polyps are in the rectum, within the reach of the proctosigmoidoscope, and can be readily removed. The following suggestions may prove helpful in clinical diagnosis.

1. The presence of mucus in the stools should precipitate a vigilant and repeated search for a polyp.

2. The intermittent occurrence of blood on or in the stool or on the tissue should raise the index of suspicion.

3. Whenever there is an indication for a Barium Enema there is an indication for an Air Contrast Study.

4. Reluctance to accept negative single X-ray studies when clinical suspicion is high.

5. Colotomy with colostomies whenever a tumor has been identified at any one site should be mandatory. (Figure V) As many as 20 per cent more lesions<sup>17</sup> have been found through colonoscopy at time of surgery than were demonstrable by X-ray preoperatively.

Once the polyp or polyps have been identified and removed, these patients should be followed carefully, since they have an 8-15 per cent chance of developing secondary or tertiary lesions. A highly recommended program includes proctosigmoid-

oscopy every six months and a Barium Enema with Air Contrast Study once a year.

**Conclusion**

Some present concepts of cancer of the large bowel have been presented. Presently it is not only the most common cancer in the United States but also appears to be on the increase. In addition, it unfortunately frequently attacks the patient in the prime of his life.

Improvement in the survival rate remains primarily dependent on early diagnosis despite recent technical advances.

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# Cancer Of The Bladder

**Bernard Lytton, M.D. and B. Marvin Harvard, M.D.**

■ Malignant tumors of the bladder are the cause for some 8,000 deaths annually in the United States and about 150 a year in Connecticut. They account for about 12 per cent of the incidence of all cancers in males and 5 per cent in females.<sup>1</sup> The corresponding figures for the death rates are 4 per cent and 2 per cent indicating an overall favorable survival rate. Bladder cancer occurs most frequently between 60 and 80 years of age and affects men two to three times as commonly as women. There has been a significant increase in the incidence of the disease in Britain and Denmark over the past twenty years, particularly among younger males,<sup>2</sup> but in the United States the increase has been only slight. (Figure I) It is of interest that this change has been more noticeable in urban as opposed to rural areas and is reminiscent of a similar but more marked increase which has occurred in lung cancer.<sup>3,4,5</sup>

## **Etiological Factors**

Cancer of the bladder is unique in that spontaneously occurring tumors and those arising from exposure to industrial carcinogens are clinically and pathologically indistinguishable. This has led to a great deal of interesting and useful experimental and epidemiological study of this disease, which has added much to our understanding of the pathogenesis, and to the elimination of a number of industrial hazards which cause bladder tumors. The latter represents one of the most significant advances in the prevention of cancer.

Seventy years ago the first three cases of bladder tumor, occurring in men engaged in the manufacture of fuchsin dye, were reported by Rehn from Frankfurt am Main in Germany.<sup>6</sup> Nine years later a further twenty-three cases were described in aniline dye workers.<sup>7</sup> Since that time there have been many reports of bladder tumors arising in individuals employed in the manufacture of aniline dyes and certain other organic compounds. Recently, however, a careful retrospective study of all affected individuals engaged in the dyestuff industry during the past fifty years, indicated that it was not the aniline dyes but certain intermediate products in their manufacture, namely alpha- and beta-naphthylamine and benzidine, that were the carcinogenic agents.<sup>8</sup> The most potent of these is beta-naphthylamine, and recently several instances of bladder cancer have been found in persons engaged in the rubber and electric cable in-

dustry where beta-naphthylamine was found to be present in an antioxidant used in the vulcanisation of raw rubber.<sup>9,10</sup> Xenylamine (4-amino-diphenyl), used in the manufacture of certain organic chemicals, appears to be another powerful carcinogen which caused an epidemic of bladder cancer in one factory, where over 11 per cent of the men exposed developed tumors.<sup>11</sup> A follow up study of these employees five years later revealed that several more had developed bladder lesions.<sup>12</sup> It has been established that these chemically induced cancers may appear anywhere between one and forty years after contact with the carcinogen with an average induction time of eighteen years.<sup>13</sup> Tumors may arise many years after the individual has ceased to be employed in the chemical industry so that prolonged and careful observation is necessary of all persons who have been exposed to a known chemical carcinogen at any time. It is estimated that there is a thirty fold increase in the incidence of bladder cancer in these individuals. As a result of these observations the chemical carcinogens have either been modified to render them harmless, or their use has been discontinued. Observation of workmen at risk is presently carried out by routine exfoliative cytology of the urine at frequent intervals and has been found to be a satisfactory screening test.<sup>14</sup> The finding of suspicious cells is followed up by cystoscopic examination and it is interesting to note that cytological abnormalities may be detected months or years before visible lesions appear.<sup>15</sup>

Several studies have indicated that smoking is related to bladder cancer in men. A prospective study carried out in the United States showed that the disease occurred three times as frequently in men who smoked more than 20 cigarettes per day as compared to nonsmokers.<sup>16</sup> An extensive survey of 369 cases of bladder cancer in Copenhagen showed a significant association between excessive tobacco consumption and the development of bladder tumors,<sup>4</sup> although in none of the studies has this been as striking as the relationship to lung cancer. A 50 per cent increase in the urinary out-

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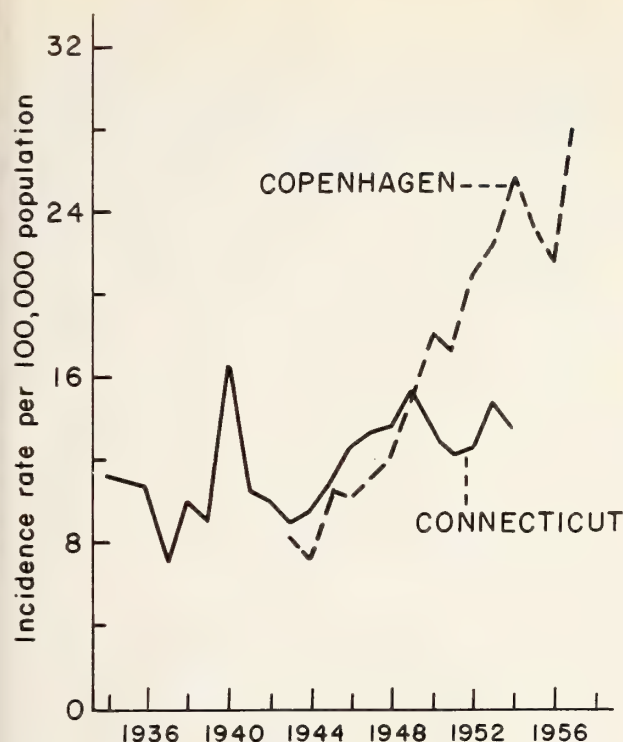


FIGURE I

i. Shows a comparison of the increase in incidence of bladder cancer in Copenhagen, Denmark and State of Connecticut.

put of carcinogenic substances, derived from tryptophan, has been detected in the urine of smokers, which apparently returns to normal levels when smoking is discontinued.<sup>17</sup>

Experimental evidence indicates that the effect of the carcinogen is mediated by its presence in the urine and that it is specific for the urinary epithelium. Dogs fed on beta-naphthylamine with the ureters implanted in the bowel do not develop tumors.<sup>18, 19</sup> Similarly fed animals in whom the bladder has been divided into two separate pouches with an intact blood supply, but where only one pouch receives urine, develop tumors only in the one in contact with the urine.<sup>20</sup> Instillation of urinary extracts, derived from patients with recurrent bladder tumors, into isolated bladder pouches in rats has resulted in the development of papillary tumors in 50 per cent of the animals.<sup>21</sup>

Extrapolating from these observations on urinary carcinogens, both in industry and experimental animals, it has been suggested that the spontaneous tumors might arise from the presence in the urine of naturally occurring metabolites which could act as carcinogens.<sup>22</sup> Breakdown products of tryptophan, chemically closely related to the industrial carcinogens and which are capable of inducing tumors in experimental animals, have been found in increased amounts in the urine of patients with

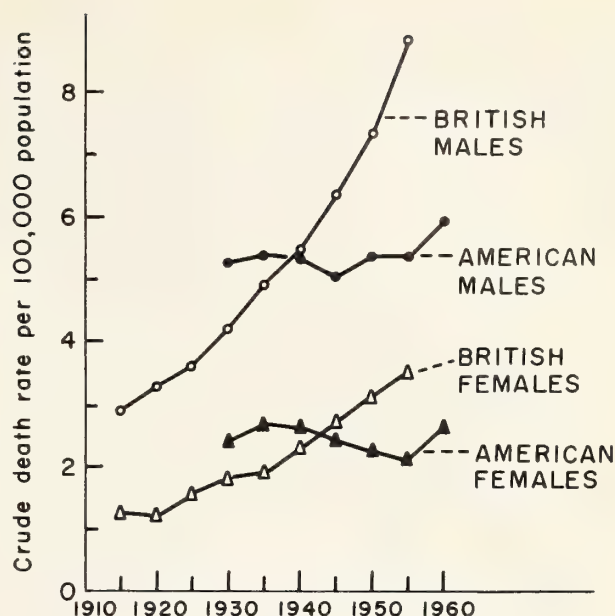


FIGURE I

ii. Shows the death rates from bladder cancer in Britain and the United States during the past forty years.

Note the marked increase among British males as compared to only a slight increase among American males.

bladder tumors.<sup>23</sup> These normally appear in the conjugated form as glucuronides, but in the urine of patients with tumors there is an increase in glucuronidase, an enzyme which liberates the carcinogen by hydrolysis. This concept led to the trial of a glucuronidase inhibitor, saccharolactone, in an attempt to prevent the recurrence of bladder tumors.<sup>24</sup> This, unfortunately did not prove to be successful but the theory may still have some validity and alternative chemical pathways are being investigated.

The role of stasis and chronic inflammation in the etiology of bladder tumors is still undetermined. It is known that in Schistosomiasis, where the ova are deposited in the bladder mucosa and produce chronic inflammatory changes, there is a relatively high incidence of cancer.<sup>25</sup> In Egypt, where Schistosomiasis is endemic and affects about 60 per cent of the population, it is estimated that bladder cancer accounts for 7.5 per cent of all deaths from cancer as compared to 3 per cent in the United States.<sup>26</sup> Jewett found evidence of stasis or vesical irritation in 47 of 80 patients with infiltrating vesical tumors.<sup>27</sup> The significance of this observation is difficult to evaluate as it is usually not possible to determine whether the infection preceded or followed the development of tumor. Occasionally patients who have what appears to be a chronic cystitis subsequently develop carcinoma of the bladder after a few years, and this should be remembered as a possible way in which the disease

can present.<sup>28</sup> The relationship of chronic interstitial cystitis to tumor formation is unclear but there seem to be a small number of patients with this condition who develop carcinoma of the bladder after a variable period of time.<sup>29,30</sup> Adenocarcinoma is a rare lesion in the bladder accounting for only 1 to 2 per cent of all tumors, and is associated with cystitis glandularis, which presents as non-translucent cyst-like lesions in the base of the bladder. The condition probably results from a cystic degeneration in the subtrigonal cell nests of Von-Brun or may originate, in cases of chronic trigonitis, from down growths of hyperplastic transitional epithelium, which then become pinched off by the surrounding connective tissue reaction. It has also been suggested that these nests may arise from aberrant urethral glands and therefore represent embryological rests. Adenocarcinoma is the commonest type of tumor found in patients with untreated vesical extrophy and it is in these bladders, which are subjected to repeated irritation from trauma and infection, that cystitis glandularis is also most frequently seen.<sup>31</sup> A high incidence of chronic urinary obstruction due to urethral stricture has been noted in Uganda Africans with bladder tumors.<sup>32</sup> It is not clear, however, what the incidence of this locally endemic condition of urethral stricture is among the general population, and again it is difficult to evaluate the significance of this observation.

### Pathology

A classification and appreciation of the pathological characteristics and natural history of bladder tumors is necessary to provide a rational basis for treatment and prognosis. The vast majority are epithelial tumors, mesenchymal tumors accounting for only 0.3 per cent.

The epithelial tumors can be divided into two major groups. First, the non-invasive, well differentiated, papillary transitional cell tumors or so called benign papillomata. These should be considered potential cancers as 15 to 20 per cent subsequently develop malignant changes and it is impossible to predict which ones will do so.<sup>33</sup> They constitute about a third of all bladder tumors, are frequently multiple and about 50 per cent of them recur after treatment, often in another area in the bladder. This multifocal origin suggests either a predisposition of the mucosa to neoplasia or the presence of a urinary carcinogen. Follow up cystoscopy at intervals of three to six months is therefore essential.

The second group are the primary malignant tumors which may be papilliferous, solid or ulcerating. The cellular configuration may be transitional, papillary, squamous (epidermoid), or anaplastic (undifferentiated), in order of frequency.

Tumors are graded 1 to 4, according to their degree of cellular differentiation but in over half of them this is very variable. The most important single feature from the aspect of prognosis and treatment is the degree of invasiveness which is found to be closely correlated with the incidence of lymphatic metastases.<sup>34</sup> This provides the basis for the classification of bladder cancer; superficial involving mucosa and submucosa (group 0 and A), invading the bladder muscle (group B), the perivesical tissues (group C), and cases with distant metastases (group D). The International Union against Cancer, an organization subscribed to by this and most other countries concerned with the classification and collection of world wide data on all aspects of cancer, has established a nomenclature, applicable to all forms of cancer, known as the T.N.M. classification where T stands for tumor stage as assessed by clinical observation, N for nodes and M for metastasis. Symbols such as S denote superficial tumors and P replaces T when the staging is done by pathological examination. This classification when generally accepted will provide for a unified system which will facilitate the world wide evaluation of the epidemiological and therapeutic aspects of malignant disease. It has been approved by the Joint Committee on Cancer staging and end results reporting in the United States and has been adopted for use in several major types of cancer already. Superficial well differentiated papillary tumors confined to the epithelial layer without invasion of the base membrane are therefore classified as S1 (group 0); involvement of the submucosa T1 or P1 (group A); invasion of the superficial muscle layers T2 or P2 (group B); deep muscle or perivesical spread T3 or P3 (group C), and fixation to surrounding structures T4 or P4 (group D). N+ indicates involvement of the regional lymph nodes and M denotes the presence of distant metastases. (Figure 2)

It has been observed that there is a distinct deterioration in the prognosis once the tumor extends more than half way through the bladder muscle. Squamous cell and adenocarcinomata are associated with a poorer prognosis than transitional cell tumors. This is further influenced by the degree of cellular differentiation. Occasionally a tumor will invade the submucosal and perivesical tissues extensively while producing only a small area of edema in the overlying bladder mucosa. These have been referred to as "iceberg tumors" and have a poor prognosis principally because of the delay in diagnosis.

### Symptomatology And Clinical Findings

Painless hematuria is the presenting symptom in nearly 80 per cent of bladder tumors and over half



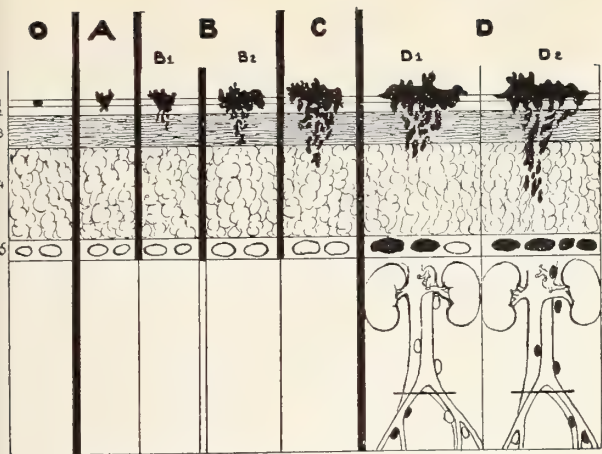


FIGURE II

Classification of bladder cancer according to degree of invasion. (After Marshall, V.F.)

of the remainder have hematuria in association with dysuria and frequency. In a small number of patients, frequency and dysuria may be the only presenting symptoms. Pain, uremia, and the effects of metastases are the initial findings in only 2 per cent of patients. The main dissemination of bladder cancer is to the regional lymph nodes and the perivesical tissues. Distant metastases are relatively uncommon and as a rule occur late in the progress of the disease. Occasionally carcinomatous peripheral neuropathy and myopathy occur, as is more commonly seen with lung cancer. This complication produced distressing symptoms in one of our patients who had undergone ureterosigmoidostomy, as incontinence developed when the anal sphincter became involved.

The importance of prompt cystoscopic and radiographic investigation of painless hematuria cannot be over emphasized in order to detect early and curable lesions. There appears to be a marked deterioration in survival rate when treatment is delayed for as short a time as one month after the onset of bleeding.<sup>35</sup> (Figure 3) There is an improvement in prognosis which occurs with further delay and this almost certainly indicates the biological relationship between tumor and host, that is to say that only those cases in whom the relationship is a good one, survive the initial period without treatment. This improvement in the prognosis in the surviving group in relation to the duration of symptoms has also been observed in the case of cancers of the stomach, lung, and colon.<sup>36, 37, 38</sup>

The diagnosis is established in most cases by cystoscopy and transurethral biopsy. This is usually performed in the investigation of the patient with symptoms but would be impractical as a screening test. Exfoliative cytology of the urinary sediment

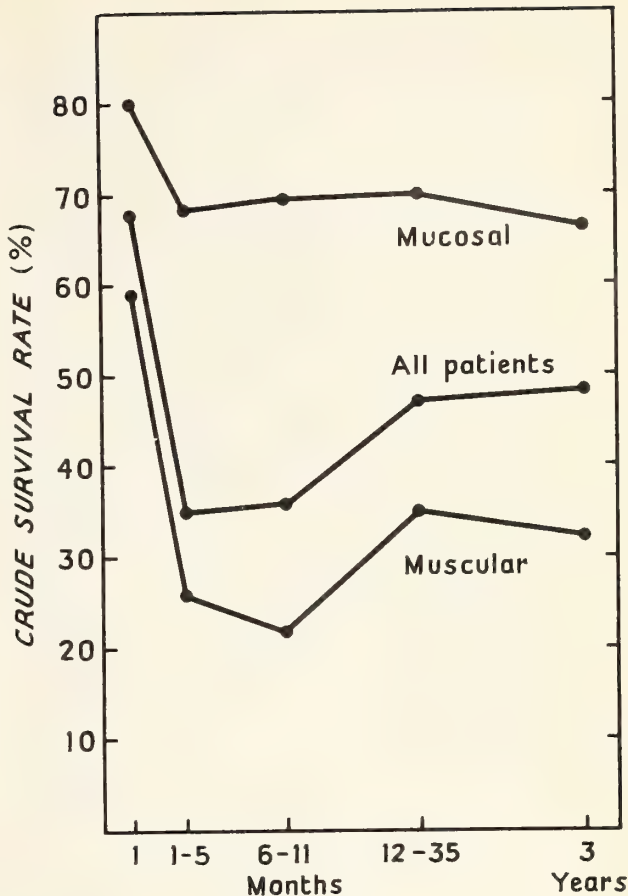


FIGURE III

Shows the five year survival rate in relation to the duration of haematuria prior to treatment. (After Wallace, D. M. and Harris, D. L.)

by the Papanicolaou technique was extensively reviewed in 1958 and it would appear that it is of definite value.<sup>39</sup> Its use as a satisfactory screening test in dyestuff workers has already been mentioned.<sup>14</sup> Failure to detect abnormal cells in the presence of an invasive transitional cell tumor occurs in about 6 per cent to 8 per cent of cases when the urine is examined by an experienced cytologist. The incidence of failure is 27 per cent in the squamous cell and non-invasive tumors.<sup>40</sup> Malignant cells were detected in the urinary sediment in 25 of 91 patients with early tumors prior to the development of any symptoms or microscopic hematuria.<sup>14</sup> Several cases have been reported in whom malignant cells appeared in the urine several months before lesions were detected at cystoscopy.<sup>41</sup> It is generally agreed that the method is valueless for the detection of the low grade papillomata as the cells cannot be differentiated from those of the normal bladder epithelium. There is some evidence that Cytology is useful in the follow up of treated cases of bladder cancer and for the detection of carcinoma in situ. Attempts to

produce fluorescence in malignant cells in the urinary sediment with tetracyclines have been unsuccessful.<sup>42</sup> The use of an ultraviolet light cystoscope to detect early malignant lesions in the bladder mucosa which have been made to fluoresce, by the administration of tetracyclines or local instillation of acridine orange, shows promise as it has been reported that several early tumors not seen on cystoscopy with incandescent light have been detected by this method.<sup>43</sup>

Excretory urography must be performed in all cases of bladder tumor to detect any co-existing lesions in the renal pelvis or ureter as these are more common in the presence of bladder tumors. The urogram will also delineate any ureteral obstruction which, if present, is indicative of invasion by the tumor as the mucosal lesions do not produce obstruction even when they arise in the vicinity of the ureteral orifice. Bimanual examination of the bladder under general anesthesia together with endoscopic biopsy enables a fairly accurate assessment of the extent of the tumor to be made.

Arteriography of the bladder combined with intravesical injection of CO<sub>2</sub> to determine the degree of invasiveness has met with only limited success,<sup>44</sup> but in some cases may be helpful in demonstrating extravesical extension.<sup>45</sup>

Lactic acid dehydrogenase (L.D.H.) is an enzyme associated with the anaerobic glycolysis which occurs in malignant tumors and is, therefore, generally present in increased amounts in the urine in the presence of established cancers of the urinary tract. Measurement of the urinary L.D.H. has been suggested as a screening test for such tumors,<sup>46</sup> but its value in this respect appears to be limited. A significant number of false negatives occur particularly with small tumors, which produce only small quantities of the enzyme, and levels are frequently elevated in other non-malignant conditions, notably infections.

### Treatment

There are a variety of methods advocated in the treatment of bladder cancer, unfortunately, in the more advanced lesions none of them has proved to be wholly satisfactory. Surgery, irradiation and chemotherapy, alone or in combination, are all useful modalities at present available. The ideal method, however, for the treatment of the individual patient depends on many factors and even after careful evaluation may be difficult to determine. The age, general condition of the patient, his life expectancy and symptomatology, together with an estimate of the immediate future course of the tumor, must be taken into consideration when deciding between curative therapy and palliation. It should be remembered that palliative treatment

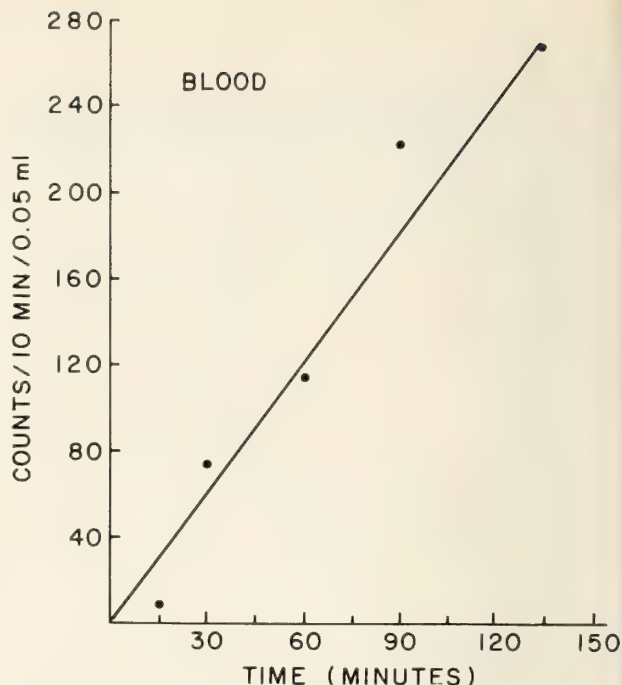


FIGURE IV

Shows the rate of absorption of thio-tepa, tagged with radioactive S<sub>35</sub>, through the bladder mucosa.

will produce a better chance of limited survival in comfort in the elderly and debilitated patient, than an overly aggressive radical approach with its attendant high mortality and morbidity. Certain broad principles we favor in the management of bladder tumors are described below.

Superficial tumors are most satisfactorily controlled by transurethral fulguration with careful follow up by cystoscopy at intervals of three to six months. When these tumors are multiple and recur frequently, good results have been obtained by the repeated local instillation into the bladder of an alkylating agent, thio teпа.<sup>47, 48</sup> Absorption of the drug does occur to some extent through the vesical mucosa (figure 4), but the amount is probably insufficient to produce a significant tumoricidal effect although reversible bone marrow depression has been reported in a few instances. Adequate control of the lesions has been achieved in 50 to 60 per cent of patients treated. Favorable results have also been reported following intravesical application of 5 per cent to 30 per cent podophyllin in mineral oil.<sup>49, 50</sup> Total cystectomy becomes necessary when control cannot be achieved by these methods. Destruction of the mucosa by cautery, the application of absolute alcohol and stripping of the bladder epithelium has been performed, apparently with some measure of success, but is associated with a considerable post-operative morbidity.<sup>51</sup> Radiation therapy yields poor results in these generally well



differentiated lesions and only adds to the morbidity of subsequent surgical procedures.

Carcinomas showing early invasion of the submucosa, and superficial muscle layers, which do not involve the base of the bladder and are solitary, are suitable for partial cystectomy. The resection should include a healthy mucosal margin of 2 cm. Ultraviolet fluorescent cystoscopy may prove useful to detect the presence of *in situ* malignant lesions in other areas of the bladder which would contraindicate local excision. Supervoltage external irradiation may provide a satisfactory alternative or may be given as adjuvant therapy. Tumors of this type in the vicinity of the bladder base are effectively treated by local excision and fulguration, either transurethrally or by a suprapubic approach depending on the size, followed by direct implantation of some radioactive source, such as radon seeds, gold grains or tantalum wire, to provide a concentrated and well localized dose of irradiation to the area immediately surrounding the tumor.

The more extensive growths involving the bladder base and deeper muscle layers or with early extravesical spread, have generally been subjected to radical cystectomy. The proximal urethra should also be excised as a recurrence rate of 4 per cent has been reported in the remaining urethra.<sup>52</sup> Urinary diversion into the colon, with implantation of the ureters in a submucosal tunnel to prevent reflux, is preferred provided there is no evidence of renal impairment or hydronephrosis. The ability of the anal sphincter to contain fluid must be assessed prior to surgery by the slow instillation of 200-300 ml of normal saline into the rectum. A tendency to hyperchloremic acidosis can usually be adequately controlled by the oral administration of sodium bicarbonate. If electrolyte imbalance or infection subsequently become a serious problem, or there are signs of renal insufficiency preoperatively, a terminal left iliac colostomy can be performed leaving the patient with an isolated rectal pouch as a urinary reservoir. This has proved to be more satisfactory than the ileal conduit as the urine is under sphincteric control and the colostomy presents fewer problems in management for the average patient than does a urinary stoma.

Construction of a sigmoid or ileal bladder substitute has been employed in two of our patients. This consists of anastomosing the mid-portion of an isolated loop of intestine to the divided urethra and implanting the ureters into the two free ends.<sup>53</sup> Patients have been found to be continent by day but have to wear either a penile clamp or an incontinence appliance at night as the external sphincter, which is a voluntary muscle, relaxes when the patient is asleep. Furthermore, the intestinal pouch unlike the bladder, is constantly under-

going peristaltic activity which leads to the passage of urine unless sphincter tone is maintained. It is recommended that this procedure should only be undertaken in carefully selected patients.

These major surgical procedures have a mortality of between 6 per cent and 12 per cent and about half the patients have some non-fatal complication in the post-operative period. Total pelvic exenteration has nearly twice the mortality of that associated with radical cystectomy, and results in little improvement in long-term survival; it is therefore no longer advocated.<sup>54</sup>

Supervoltage irradiation with a cobalt 60 source or a linear accelerator, which allows curative doses to be given at an optimum depth without significant injury to the skin and superficial tissues, has given promising results.<sup>55, 56</sup> Patients are given 6,000 R to 7,000 R over periods of five to seven weeks for curative treatment and 3,000 R to 4,000 R over two to three weeks for palliation. Intracavitary irradiation is more difficult to administer, yields less satisfactory results and is attended by a greater morbidity. Urinary infections should be eradicated before commencing treatment as it is associated with an increased morbidity. Mortality is low and in many adequate bladder function is preserved. Unfortunately, there is a significant degree of morbidity affecting about 25 per cent of patients treated. In one-third of these it is prolonged, is sometimes permanent and in a few ultimately fatal. The principal complications are hematuria, which may be severe and persistent due to telangiectasia; bladder contracture (with loss of 25 to 75 per cent of capacity) and cystitis causing various degrees of frequency, fistula formation and renal failure from ureteral obstruction and infection. Enteritis and proctitis may occur and the latter can be severe enough to warrant a colostomy. The residual bladder symptoms may be severe enough to require urinary diversion.

The need for urinary diversion should be anticipated whenever possible and be carried out prior to irradiation therapy. There is evidence to suggest that urinary diversion together with irradiation yields better results than irradiation alone.<sup>52</sup> Ureterosigmoidostomy is unsuitable when heavy doses of irradiation have been administered due to the frequently associated proctitis and in these cases ileal loop diversion with high anastomosis of the ureters is recommended. The vascular impairment following such irradiation results in poor healing with a high incidence of fistula formation.

The results of treatment expressed in terms of five-year survivals are similar for most methods currently used. Comparisons between surgery and irradiation are difficult because in the former staging of the tumor's progress follows a pathological clas-

sification while in the latter a clinical classification is used. Nevertheless, there is an overall survival rate of about 25 per cent for either method. It has been clearly shown that the single most important prognostic factor is the extent of invasion of the bladder muscle, there being a sharp decrease in the likelihood of survival once the tumor has penetrated more than halfway through the bladder wall.<sup>58</sup> Following surgical resection the five-year survival rate falls from 50 to 70 per cent in superficially infiltrative lesions to between 15 to 5 per cent in the deeply invasive lesions. Extravesical extension and local lymphatic metastases further reduce the survival rate to four per cent or less.

It appears that in the deeply invasive tumors an improvement in the results may be obtained by pre-operative irradiation with about 4,000 R followed by the radical cystectomy four to eight weeks after completion of treatment. The three-year survival rate of 19 patients so treated was increased from 22 per cent to 42 per cent by such combined therapy and other reports have been encouraging.<sup>57</sup> There is, however, a significant increase in the morbidity after this type of treatment due to serious wound infections, dehiscence and the development of urinary fistulae. Radiation followed by diversion with or without cystectomy is also the treatment of choice in cases of bladder cancer which have recurred following conservative surgery.

Chemotherapeutic agents have been used principally for palliation apart from the local application of thio-tepa in superficial tumors. The anti-metabolite 5-fluoracil has been found to be the most effective agent in the treatment of transitional cell tumors.<sup>59</sup> Administered intravenously it produces evidence of tumor regression in about 30 per cent of cases but for a short period and only for a few months. Intra-arterial infusion directly into the internal iliac arteries has resulted in good palliation with objective evidence of tumor regression and relief of pain for periods up to six months and has produced a further brief remission after recrudescence of tumor following irradiation.<sup>60</sup>

Encouraging preliminary results have been reported with the combined use of 5-fluoracil intravenously and supervoltage irradiation followed by radical surgery in selected cases.<sup>61</sup>

The foregoing discussion demonstrates clearly that despite some encouraging advances in therapy that except in small superficial well differentiated tumors, the treatment of bladder cancer is far from satisfactory. No single method is all embracing and each may have serious disadvantages. In choosing a plan of treatment each patient must be studied carefully and approached as an individual therapeutic problem. The plan should provide, if pos-

sible, the greatest opportunity for cure but must also encompass such calculations as life expectancy, type and stage of the tumor, as well as the direct and indirect effects of the modality employed.

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# The Usefulness Of The Connecticut Central Tumor Registry

Henry Eisenberg, M.D., M.P.H.

## Historical Introduction

■ The General Assembly of the State of Connecticut in 1935, passed a bill at the request of the State Medical Society which authorized the State Department of Health to establish a Division of Cancer Research. The Division was charged with the responsibility of fulfilling a mandate given to it by the legislature which requested that the State Department of Health "make investigations concerning cancer, the prevention and treatment thereof, and the mortality therefrom, and to take such action as it may deem will assist in bringing about a reduction in the mortality due thereto." Since its establishment in 1935, the Connecticut Tumor Registry has grown and matured in various ways. The number of cancer cases reported to the Connecticut Tumor Registry by the various general hospitals in the state of Connecticut, had increased by 1964, to approximately 170,00 tumors. Since the reporting of tumors found in patients living in the state of Connecticut is almost 100 per cent, the Connecticut Tumor Registry is based on the total population of the state of Connecticut and, therefore, is capable of providing information concerning the size and the nature of the cancer problem in the state. In addition, it makes it possible to develop indices for evaluating the progress made in bringing cancer in the state of Connecticut under control. Data on the number of cancer patients reported in the state permit the development of incidence rates by age, sex, type of tumor, site of tumor, and various other variables. It further produces information on trends in cancer incidence, stage of disease at diagnosis, and, of great importance, survival experience of patients from various treatment methods. Information resulting from the analysis of the data in the Register should serve to arouse and maintain interest in the fight against cancer and, at the same time, provide knowledge for guidance of the therapeutic approach to various types of cancer to the medical profession in Connecticut.

The operations of the Connecticut Tumor Registry have been amply described by Greenberg,<sup>1</sup> Campbell,<sup>2</sup> and Kralits.<sup>3</sup> It is using for its oper-

ations the most up-to-date IBM equipment and it continues to strive to improve its methods evermore. One of the important features of the Registry is the follow-up system. A follow-up report is received for each patient six months after discharge from the reporting hospital. Subsequent follow-up is then requested on a yearly basis as long as the patient lives. The average loss to follow-up of patients seen over these years has been less than five per cent. The complete system of follow-up has been described by Keogh.<sup>4</sup>

The Connecticut Tumor Registry is one of several registries throughout the United States most of which are hospital-based in university centers, which cooperate with the National Cancer Institute's End Results Section of the Biometric Branch to continuously evaluate the therapeutic approach to cancer treatment. Almost one hundred articles have been written to date utilizing the data derived from the Connecticut Tumor Registry. Besides members of the Registry staff and researchers and physicians outside of the state, a great number of physicians in Connecticut have taken advantage of the data within the Registry to write articles about various sites of cancer as seen among patients in Connecticut.

## Participation In National And International Cancer Meetings

Due to its unique position and its ability to produce incidence rates based on a total population group, the Connecticut Tumor Registry has been asked many times to contribute to cancer meetings. It contributed a variety of data to the Third, Fourth, and Fifth National Cancer Conferences and to the Eighth International Cancer Conference besides several meetings which were for specific sites of cancer in the national and international fields. Among the papers that have been presented has been one, "Secular Trends in Survival: Five Years and Later, Cancer Patients Drawn from a Defined Population—Connecticut, U.S.A.,"<sup>5</sup> which was presented at the Eighth International Cancer

*This paper is supported in part by Grant No. CA09808-05, National Institute of Health.*

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Congress in Moscow in 1962, a congress which was sponsored by the International Union Against Cancer. The Connecticut Cancer Registry is the only registry in the world which has been operating for these many years and has information available on the survival of cancer patients for 27 years as of this date. Therefore, the Registry is able to show the survival of the various types of cancer by various treatment methods which gives an indication of progress or no progress, whatever the case may be, as measured by the method employed to treat these cancers divided into other important variables. As important as survival data are, it is at times indicated to bring them into relationship with mortality data and especially incidence rates.

### Data From The Registry

The first comprehensive report was published in 1955, by Griswold, *et al*,<sup>6</sup> which contained information taken from the Central Tumor Registry. Described in detail among others was information on the trend in cancer incidence by sex and site, the variations therefrom, the stage of disease at diagnosis, and the survival by treatment. All these data were based on a total population group, the state of Connecticut, and used actuarial or modified life-table methods for the computing of survival rates. This information, in general, presented the size and the nature of the cancer problem and describes the changes which had taken place over the period of 17 years. It demonstrated "several kinds of information which a register is designed to produce without going back into clinical records for additional detailed data."

In describing the survival rates of various sites of cancer, divided into time periods by age, sex, stage of disease, and type of treatment, the monograph expressed the survival experience of the average cancer patient for this particular type of cancer as diagnosed and treated in Connecticut hospitals.

In 1964, the Registry published a monograph, "Cancer in Connecticut—Mortality Data, 1949-1961,"<sup>7</sup> with an addendum, "Cancer in Connecticut—Supplementary Mortality Data, 1949-1962,"<sup>8</sup> (in print) which describes the number of deaths from cancer and other malignant tumors by numerous variables.

Two additional yearly monographs<sup>9,10</sup> were published in 1960 and 1961, respectively. The Connecticut Tumor Registry is in the process of preparing an incidence monograph. From the data to be used in this monograph, the following are, as yet, some unpublished data. Table I gives the number of cases, crude and age-adjusted incidence rates per 100,000 population by sex, for cancer of all sites in Connecticut for the last 28 years. When

TABLE I  
NUMBER OF CASES, CRUDE AND AGE-ADJUSTED<sup>1</sup> INCIDENCE  
RATES PER 100,000 POPULATION BY SEX, FOR CANCER  
OF ALL SITES  
CONNECTICUT 1935-1962

| YEAR OF<br>DIAGNOSIS | NUMBER | SEX           |                          |               |                          |       |
|----------------------|--------|---------------|--------------------------|---------------|--------------------------|-------|
|                      |        | MALES         |                          | FEMALES       |                          |       |
|                      |        | CRUDE<br>RATE | AGE-<br>ADJUSTED<br>RATE | CRUDE<br>RATE | AGE-<br>ADJUSTED<br>RATE |       |
| 1935                 | 1407   | 170.2         | 196.1                    | 1853          | 222.2                    | 236.2 |
| 1936                 | 1398   | 168.1         | 192.7                    | 1777          | 211.8                    | 221.3 |
| 1937                 | 1383   | 165.3         | 185.9                    | 1822          | 215.7                    | 221.1 |
| 1938                 | 1531   | 181.9         | 201.0                    | 1863          | 219.2                    | 222.3 |
| 1939                 | 1578   | 186.5         | 202.6                    | 1921          | 224.6                    | 224.2 |
| 1940                 | 1641   | 192.8         | 206.7                    | 1930          | 224.3                    | 221.0 |
| 1941                 | 1689   | 192.9         | 201.7                    | 1990          | 224.6                    | 216.7 |
| 1942                 | 1801   | 198.7         | 204.4                    | 2083          | 227.0                    | 215.3 |
| 1943                 | 1807   | 194.6         | 197.6                    | 2159          | 229.7                    | 216.4 |
| 1944                 | 1933   | 205.5         | 206.4                    | 2228          | 233.8                    | 217.8 |
| 1945                 | 2005   | 212.0         | 211.3                    | 2272          | 237.0                    | 219.0 |
| 1946                 | 2156   | 226.6         | 224.0                    | 2251          | 233.4                    | 213.7 |
| 1947                 | 2202   | 229.5         | 227.1                    | 2506          | 257.7                    | 235.6 |
| 1948                 | 2427   | 251.1         | 248.2                    | 2744          | 279.7                    | 254.8 |
| 1949                 | 2499   | 254.3         | 249.2                    | 2730          | 273.7                    | 248.2 |
| 1950                 | 2588   | 260.6         | 251.2                    | 2822          | 275.8                    | 246.0 |
| 1951                 | 2687   | 266.0         | 257.4                    | 2852          | 273.7                    | 245.2 |
| 1952                 | 2815   | 271.6         | 262.9                    | 3116          | 291.3                    | 259.6 |
| 1953                 | 2930   | 274.1         | 264.3                    | 3145          | 284.9                    | 252.7 |
| 1954                 | 3122   | 282.6         | 271.7                    | 3209          | 281.0                    | 247.3 |
| 1955                 | 3189   | 282.3         | 273.7                    | 3243          | 277.6                    | 244.6 |
| 1956                 | 3363   | 292.2         | 282.8                    | 3500          | 293.9                    | 260.8 |
| 1957                 | 3452   | 293.7         | 283.9                    | 3443          | 282.9                    | 248.4 |
| 1958                 | 3624   | 300.5         | 290.3                    | 3730          | 298.5                    | 261.5 |
| 1959                 | 3799   | 309.7         | 299.0                    | 3790          | 298.0                    | 262.0 |
| 1960                 | 3901   | 312.5         | 302.6                    | 3816          | 294.6                    | 257.5 |
| 1961                 | 3762   | 294.4         | 286.2                    | 3915          | 295.2                    | 261.7 |
| 1962                 | 3792   | 290.2         | 281.9                    | 4007          | 295.5                    | 262.6 |

<sup>1</sup> Adjusted on the Total Population of the Continental United States, 1950.

looking at these figures it should be kept in mind that the data are adjusted on the total population of the Continental United States for the year of 1950. The age-adjusted rate for men in 1935 was 196, while in 1962 it was 282 or a 43.8 per cent increase. For women the increase was only 11 per cent from 1935, with age-adjusted rates of 236 to 1962, when it was 263.

Most of the papers that have been written from data derived from the Central Tumor Registry by Connecticut physicians are based upon survival experience of patients with cancer of certain sites.

Ottenheimer and Oughterson<sup>11</sup> published an observation on cancer of the colon and rectum in Connecticut based on an analysis of 5,572 proven cases which were derived from data taken from the Registry after it had been operating for a period of 19 years. It was the observation of these surgeons that there had been a slow but real progress in the

management of cancer of the rectum and colon over these years. It was their belief that this improvement was greatly based upon "the ability of more and more surgeons to perform radical operations with a steadily decreasing mortality."

In 1964, Kuehn and others<sup>12</sup> reported on the epidermoid carcinoma of the perianal skin and anal canal which included a review of 157 cases taken from the Connecticut Registry material since 1935. The in-depth study of this type of cancer demonstrated again the usefulness of the data within the Connecticut Tumor Registry and permitted the authors to discuss the ideology and symptomatology as the result of treatments of various kinds given to these patients. For the very first time in this type of a large series of cases, the authors were able to determine sites of metastasis in relation to the original anatomical location of the primary site. They described the method of therapy best suited for this type of cancer and gave survival rates of those patients whose data were recorded in the Connecticut Registry over more than 25 years.

In 1964, Barnett and Eisenberg<sup>13</sup> reported on the histologic grading and survival in a large series of breast carcinoma. "The object of the study was to decide whether histologic grading of breast carcinoma was a useful prognostic tool." It was the opinion of the authors that such a tool is of great importance so that various treatment methods can well be compared by looking at five-year survival rates. Five thousand, seven hundred and seventy patients with carcinoma of the breast treated in just nine Connecticut hospitals between 1935 and 1956 were used as a basis for this study. These cases had originally been graded by the Haagensen technique and it was found that there seems to "be substantial prognostic value to such grading when five and ten-year cumulative survival rates were calculated. Grading appears to be a useful endeavor which can be done on a routine basis by many pathologists and one which helps define different groups of patients with differing prognoses."

In order to provide information on the outcome of patients with cancer treated by the various hospitals in the state of Connecticut, a system of auditing such cases by individual hospitals has recently been developed. A computerized technique was used in the audit for two general hospitals which presently are evaluating their own results of the therapeutic approach to their cancer patients seen and treated by them.

Among some of the most important data that have come from the Connecticut Tumor Registry and have proved to be of the greatest value have been those which relate the survival experience of the average cancer patient in a defined population.

TABLE II  
FEMALE BREAST CANCER 5-YEAR RELATIVE SURVIVAL RATES  
AMONG CASES DIAGNOSED 1935-56 IN CONNECTICUT

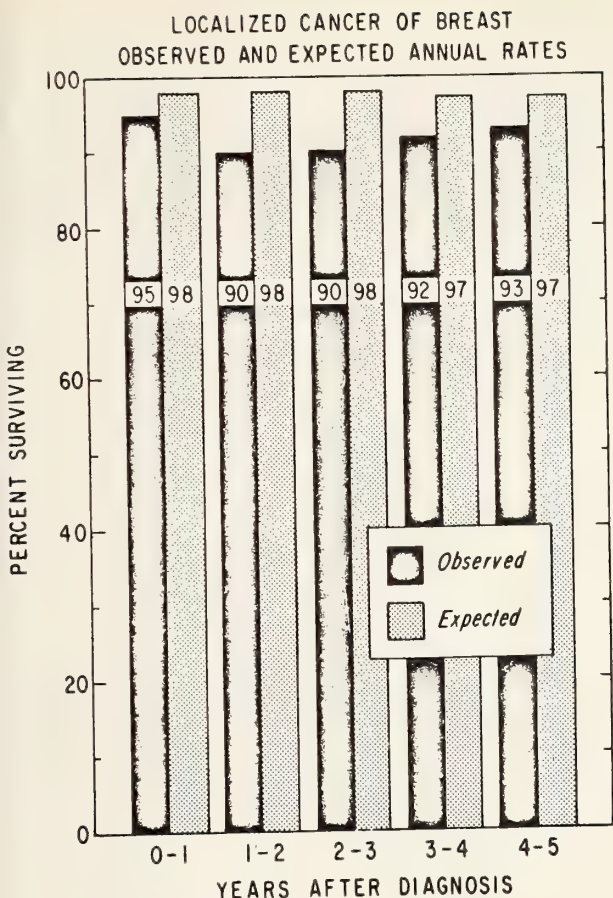
| TREATMENT         | 1935-45 |          | 1946-56 |          |
|-------------------|---------|----------|---------|----------|
|                   | CASES   | RATE/100 | CASES   | RATE/100 |
| All surgery       | 3738    | 56       | 6320    | 63       |
| Limited surgery   | 991     | 55       | 1099    | 53       |
| With radiation    | 222     | 46       | 245     | 39       |
| Without radiation | 769     | 57       | 854     | 57       |
| Radical surgery   | 2747    | 57       | 5221    | 65       |
| With radiation    | 883     | 48       | 1030    | 51       |
| Without radiation | 1864    | 61       | 4191    | 68       |

As an example, it might be well to take the survival pattern of breast cancer in women as it has been observed on a quantitative as well as qualitative basis.

Table II shows the five-year relative survival rates of 10,058 cases of breast cancer in women diagnosed in the time period between 1935 to 1956 in Connecticut. For comparison purposes, this time period has been divided in two, 3,730 cases seen in 1935-1945 and 6,320 cases reported during the period of 1946-1956. There has been an improvement of the survival rate when combining all types of surgery from 56 per cent in the first time period to 63 per cent in the second time period. However, there is a great deal of difference when these cases are divided into limited surgery and radical surgery either with or without radiation. By just looking at limited surgery alone over the two time periods, it has remained almost the same while when limited surgery with radiation is interpreted, the survival rate actually has declined from 46 per cent in the first time period to 39 per cent in the second time period. Radical surgery, taken with and without radiation combined, has improved within these two time periods from 57 per cent to 65 per cent. Only a small improvement, not statistically significant, was seen to have occurred when radical surgery was combined with radiation.

This is a brief view on the approach to the interpretation of relative survival rates of breast cancer to measure the effectiveness of this type of cancer therapy. With the data available, the information on the ten-year, fifteen-year, twenty and twenty-five-year survival of these patients originally diagnosed in the early years of the Registry could be gathered from the data available. It has been found that ten-year survivors comprise only about 60 per cent of those who had survived five years. A number which continues to be reduced when one looks at the fifteen-year survival rates of those patients with breast cancer. It may be of importance to state at this time that the method used to derive at these survival rates is called the actu-





SOURCE: CONN., 1935-44

FIGURE I

Taken from the paper, "Survival Patterns for Some Forms of Cancer," by Eisenberg, Cutler, and Axtell, published in 1964.

arial method and takes into account the normal attrition by age of all other people without cancer.

An entirely different picture of survival of breast cancer patients can be seen when one studies the analysis of data of the subsequent survival experience of five-year survivals. This becomes increasingly important when one wants to evaluate the long-term therapeutic effect on a more meaningful basis and, at the same time, look at a better understanding of the natural history of the disease. In looking at such a type of survival, one has to keep in mind that any patient with a particular form of cancer remains subject to the risk of dying from all other possible causes. One is also aware of the fact that this competing risk increases as the patient gets older. Some extensive studies were done with the data from the Connecticut Registry some time ago which produced a paper on the survival patterns for some forms of cancer.<sup>14</sup> In order to be able to accomplish such investigation, it is necessary to adjust for the risk of dying from other causes when one wishes to study the manner in

which the risk of dying from cancer changes with the time elapsed from date of the initial diagnosis or treatment. In a statistical sense, this is expressed by the ratio of the survival rate observed in a group of patients to the rate expected on the basis of general population experience and provides a measure of the probability of escaping the risk of dying from the specific cancer, in this case, breast cancer. Figure I (taken from the paper, "Survival Patterns for Some Form of Cancer," by Eisenberg, Cutler, and Axtell, published in 1964) "illustrates the basic principle in the computation of relative survival rates. This chart describes the survival experience of 1,493 female patients with localized cancers of the breast. The first pair of columns indicate that 95 per cent of the patients were alive one year after diagnosis, whereas, in the general population, in a group of women similar in age composition to the patients, 98 per cent would be expected to survive one year. The ratio, 95 over 98, indicates that 97 per cent of the women expected to survive, in fact, did survive." Figure II demonstrates what happens when one applies this particular statistical method to these types of cancer patients with breast cancer. Among patients with breast cancer, either localized or regional, diagnosed during the period 1935-1944, survival improved continuously during the first twenty years after diagnosis. There was a similar trend among patients with regional metastasis but at a lower level. A similar pattern was observed during fifteen years of follow-up of patients diagnosed in the time

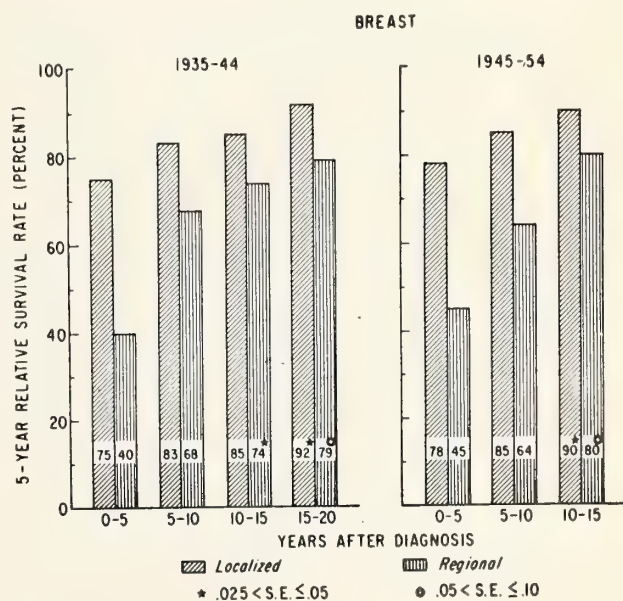


FIGURE II

Taken from the paper, "Survival Patterns for Some Forms of Cancer," by Eisenberg, Cutler, and Axtell, published in 1964.

period 1945-1954. The survival pattern for patients with breast cancer appears to be quite regular. The longer a patient has survived, the better are her chances of escaping the risk of dying from breast cancer in the next interval. Furthermore, during each five-year interval of observation the mortality risk was higher for patients with metastatic cancer than for patients with localized tumors. Without any doubt, the figures in the table and the figures given here show the importance of the data collected, and the various methods of statistical interpretation and analysis of these data. It also shows the medical profession an evaluation of therapeutic approaches.

### Quality Of Survival

Examples of this type of survival experience either for five and more years or for the first and subsequent five years can be given and are available in the Connecticut Tumor Registry. Additional studies can be made which will give not just the quantity of survival, but the quality of survival of patients. Such a study was undertaken recently with data derived from the Connecticut Tumor Registry. However, in addition to the data available, it was necessary to interview patients who had been diagnosed and operated on for breast cancer. This was done after permission was received from the private physician to contact these patients. Two hundred and fifty of these patients were thus contacted and interviewed within six to eight weeks after surgery and again between sixteen to eighteen months after surgery of those still alive at that time. Extremely interesting observations were made and described in a paper, "The Measurement of the Quality of Survival of Breast Cancer Patients in Connecticut," which recently was presented at a Breast Cancer Symposium in London sponsored under the auspices of the Imperial Cancer Research Fund.<sup>15</sup> "It was the intent of the study to evaluate the ability and capacity of the patient to resume her preoperative responsibilities whether it meant returning to outside work or to her house hold chores. Such variables as the extent of the lymphedema postoperatively and arm function as expressed by degrees were evaluated."

Some of the results obtained were as follows: "The quality of survival—was good for what can be termed the performance aspects of the patient's recovery involving arm function and activity status. It was less favorable when lymphedema of the arm was present and the attitude of the patient concerning the surgery and its aftermath were considered."

Without any doubt, quality of survival is of tremendous importance not just to the patient but also to the physician who has to consider the

therapeutic approach after the diagnosis of cancer has been made. The physician has to consider that he wishes to have his patient survive as long as possible under conditions favorable and satisfactory to the patient. As is well known, in many instances the patient survives in distress and is unable to perform functions which he or she would normally fulfill. In addition to this, suffering seems to be present in various forms and sometimes the question arises whether the physician has really helped the patient by having him live under horrible conditions.

### Summary

Studies are continuing constantly and new ones will be devised which will utilize the data of the Central Tumor Registry on a quantitative and qualitative basis. It was the intent of this paper to demonstrate certain ways data of the Central Cancer Registry can be and have been used to better achieve inside information on the natural history of the disease, on the therapeutic approach used, and its effectiveness as expressed in survival years. The trends of incidence rates over the years have been increasing, decreasing or fluctuating and have led to clues in the epidemiological approach of studies of this type of cancer. There are data in the Registry which cry for further evaluation and interpretation and the medical profession, as in the past, is again invited to make use of the data available. The Tumor Registry has proven itself to be an instrument of importance and usefulness and has achieved its status through the continuous cooperation of the medical profession who originally had the idea for such a registry and requested its formation almost thirty years ago.

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## **IMPORTANT — PLEASE READ**

**On recommendation of the Committee on Public Health, the Council adopted (1/20/65) the following resolution:**

**WHEREAS: The Committee on Public Health of the Connecticut State Medical Society has reported that the incidence of gonorrhea and of primary and secondary syphilis is on the increase, therefore be it**

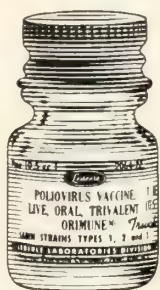
**RESOLVED: That the Council of the Connecticut State Medical Society urge that:**

**1. Each physician report every diagnosed case of gonorrhea and/or syphilis, in accordance with State law.**

**2. Each patient having gonorrhea and/or syphilis be interviewed for the purpose of determining contacts, and that such contacts be located, examined and treated whenever necessary.**

**3. Physicians utilize the service of local and state departments of health for the purpose of interviewing such patients, and for locating and following up such contacts.**

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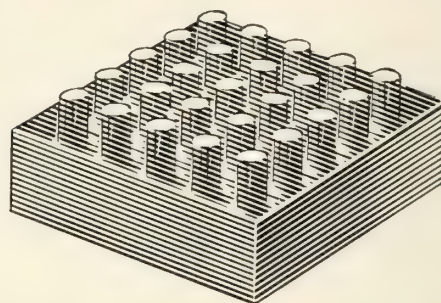
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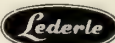
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\*Rosenthal, S. R., Nikurs, L., Yordy, E., and Williams, W.: Scientific Exhibit Presented at the Annual Meeting of the National Tuberculosis Association, Chicago, Illinois, May 30-June 2, 1965.

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# THE PRESIDENT'S PAGE

## The 174th Annual Meeting

IT is the consensus of those concerned with attempting to carry out the objectives of the Society that the 174th Scientific Assembly, held at Hartford during the last week in April, was one of the most successful in recent years. The general programs and the meetings of the Sections were well attended, the speakers responded to the enthusiasm of their audiences, and the question-and-answer periods were brisk and stimulating. The Program Committee is certainly to be commended for its efforts, and can take satisfaction for a job well done.

The associated functions of the session were also of high quality. The Connecticut Physicians' Art Association displayed a particularly fine collection of works by doctors and members of their families which elicited much interest and favorable comment. Twelve of our older colleagues were awarded certificates and pins in recognition of their fifty years of membership in the Society. Durward G. Hall, M.D., U.S. Representative from Missouri, made a stirring speech on the medical implications of current and proposed national legislation to a highly responsive group at the annual dinner. And, continuing to give us their valued support, our professional and scientific exhibitors played an important part in sustaining the cordial and informative atmosphere which characterized the affair from beginning to end.

Of special mention, I think, was the meeting of the House of Delegates. More than one hundred and twenty dedicated physicians, representing their colleagues at county and local level, spent a very full day on April 26 receiving, considering and acting upon reports and recommendations from the body's interim agents; i.e., the Council, the officers, and the many standing and special committees. Attempting to serve wisely and well the Society's more than 3600 members, the House labored diligently to do those things and adopt those policies which would merit the approval and support of the majority without bringing harm or embarrassment to those of contrary mind. We were honored by the attendance of many official visitors from our sister organizations in the New York-New England area, and, without exception, each of them brought a worthy message to present with his ceremonial "greetings." From the standpoint of fulfilling its mission as the highest governing body of the Society, it is my opinion—and one shared by many — that the House did itself proud.

Concluding on a somewhat less happy note, I was disappointed to observe how few members of the Society who were not delegates attended the business session of the House. In these days of rapidly changing medical economics, it is of the utmost importance that there exist effective two-way communications between the Society and its members. The format of meetings of our legislative assembly provides for the give-and-take of open reference committee hearings, and yet — sad to say — an audience of interested members at large is rarely present to participate in such hearings. Hence the reference committees very seldom hold forth, and it seems to me that something of real value is lost as a consequence.

In the future I would hope that all members of the Society who possibly can — whether they are in private practice or pursuing academic work — might make a sincere effort to sit in on meetings of the House and let their views be known. Exercise of this right and privilege by a greater number could make a real contribution to the discharging of the profession's responsibility to assure a high quality of medical care to the people of Connecticut. The few are often hard put to do this unassisted by the many.

ORVAN W. HESS, M.D.

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**AS MOUTHWASH OR GARGLE:** 1/2 teaspoonful in 1/2 glass of warm water several times a day.

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**\*Reference:** Litchfield, H. R.: Archives of Pediatrics, 71:367-369. Nov. 1954

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*Assistant to General Manager*

## SUMMARY OF COUNCIL ACTIONS

**Thursday, April 21, 1966**

### I. Attendance

Present in addition to the Chairman, Dr. S. J. Martin, were: Drs. Hess, Bradley, Golderg, W. Martin, Weise, Sr., M. Caplan, Brandon, H. Caplan, Pitock, Rogol, Grendon, Egan, Deming, Palumbo, Shepard, Ayres, Nolan, Cramer, Fabro, Grant, and Abbot. Also present were: Mrs. Lindquist, Mr. Chilcoat (AMA) and Dr. Richards. Absent were: Drs. Cullen, Gardner, Spitz, Ciccarelli, Petrie, Wilson, Hastings and Roch.

### II. Routine Business

#### Approval Of Minutes

It was VOTED to approve the minutes of the meeting of March 23, 1966, as printed and distributed.

#### Life Memberships

It was VOTED to approve applications for Life Membership received from the following Active Members of the Society:

Allen M. Margold, 148 East Avenue, Norwalk (FCMA) Jan. 1, 1967. E. Markey Pullen, 76 Elm Street, New Canaan (FCMA) Jan. 1, 1967. Edward Philip Kemp, 178 Reef Road, Fairfield (FCMA) 1966. Joseph Petrelli, 455 Orange Street, New Haven (NHCMA) Jan. 1, 1966.

#### Student Memberships

It was VOTED to elect to Student Membership the following Connecticut residents who are attending schools of medicine as indicated:

Paul Joseph Coppola, 183 East Grand Avenue, New Haven, Georgetown University School of Medicine — Class of 1969.

Francis Joseph Scarpa, 20 Summit Street, Derby, Johns Hopkins University School of Medicine — Class of 1967.

#### CSMS Dues Exemptions

It was VOTED to exempt from payment of 1966 CSMS membership dues the following Active Members for the reasons indicated.

Charles R. Brinkman, Capt., M.C. (NHCMA) —

Military Service; Wichard A. J. van Heuven (NHCMA) — Postgraduate Education.

#### Representative—3rd National Congress On Medical Quackery

It was VOTED to request Max Caplan, Meriden, to attend this meeting as a representative of the Society and to reimburse him for usual expenses incurred by his attendance. The Congress will be held at the Pick-Congress Hotel, Chicago, October 7-8, 1966.

#### Appointment—Representative To Connecticut Association For Mental Health

It was VOTED to appoint Frank K. Abbot, Waterbury, to serve with the Program Committee of the CAMH and, later, possibly with that organization's Board of Directors.

#### Report—Planning Committee For Seminar On Hospital Infections

Max Caplan, Meriden, serving with Stanley H. Osborn as CSMS representatives on this Planning Committee, reported on the progress which has been made in planning a Seminar on Hospital Infections to be held in April, 1967. It was VOTED to accept the report as information and to assure Dr. Caplan that, if necessary, the Society would contribute up to \$200 to help pay the expenses of one of the speakers on the program.

#### Date Of Next Meeting

In accordance with the Bylaws, the next meeting will be called by the President "as soon as possible after the annual meeting of the House of Delegates." Dr. Hess has set the date for the 1966-67 organizational meeting for Wednesday, May 25, 1966.

### III. Old, New And Special Business

#### Legal Opinion—Proposed Amendment To The CSMS Charter

Pursuant to a proposal to make past presidents of the Society *voting* members of the House of Delegates, Wiggin and Dana (the Society's attorney's) filed an opinion as follows: (a) Such a proposal would necessitate an amendment being made to the Charter; (b) An amendment to the Charter would require a Special Act of the General Assem-

bly; (c) To seek a Special Act from the Assembly for the single purpose stipulated would seem undesirable. It was VOTED to accept this advice of legal counsel and, on April 26, to recommend to the House of Delegates specifically that the proposal to make past presidents of the Society voting members of the House of Delegates be *not* approved, and that *no* Special Act of the General Assembly to amend the Charter be sought at this time.

**Question—Uniformity Of CSMS And County Association Bylaws Re "Suspension"**

Having previously (March 23) temporarily resolved an apparent conflict between the CSMS and the HCMA bylaws concerning the details of suspending a member from good standing, it was VOTED to refer this entire question (re *all* county association bylaws) to the Subcommittee to Study and Revise the Bylaws for study and report to the Council. The "details" relate to terminology, payment of membership dues, etc.

**Report—Ad Hoc Committee On Staff Structure**

After hearing the report of this Committee on its efforts to define the qualifications to be sought in a person to carry on the Society's public relations program, and to find a person having those qualifications, it was VOTED to accept the report of the Committee and to approve its recommendation that Mr. Peter F. Villano, New Haven, be engaged (on prescribed terms) as Director of Public Relations and Communications of the Connecticut State Medical Society, replacing Mr. James G. Burch, resigned. Mr. Villano will assume his duties full-time on and after June 1, 1966.

**Final Report On Medicare—Committee On Hospitals**

It was VOTED to accept, with commendation, a "final report" on its studies of the Medicare Law filed by the Committee on Hospitals. It was further VOTED to approve a recommendation contained in the report, which called for an "Ad Hoc Committee on Medicare Experience" to be formed, its functions to be to receive, evaluate, correlate and report on the experiences (problems) of physicians rendering services to patients under the Medicare Law; to assist physicians in legally and ethically resolving such problems, whenever possible; and to make recommendations to the Council concerning legislative and administrative changes in the Law to be sought from the proper agencies to eliminate such problems by deleting or amending the rules and regulations considered to be responsible for same.

It was further VOTED to direct the Chairman, after the 1966 election of committees by the CSMS House of Delegates, to promptly appoint such an

Ad Hoc Committee in accordance with the recommendations contained in the report, and to take steps to inform all physicians that a committee is operative for the purposes stipulated.

It was further VOTED to disband, with thanks, the "Committee on Medicare Planning (Medicare-Type Legislation)" which had been appointed on a temporary basis in February, 1965, prior to the enactment of P.L. 89-97.

**Report—Advisory Committee To State Commissioners Of Welfare, Finance and Control**

It was VOTED to accept a report of this Advisory Committee (augmented by representatives of the Committee on Third Party Payments and the Council), and to approve a resolution contained therein (somewhat edited) as follows

BE IT RESOLVED: That if Welfare Commissioner Shapiro will, in his Department's 1967 budget, incorporate funds sufficient to cover the expense of paying doctors of medicine on the basis of their usual and customary fees under Title XIX of P.L. 89-97, the Connecticut State Medical Society will support such a budget and do all things possible to obtain its approval by the General Assembly, and be it further

RESOLVED: That it be reiterated to Commissioner Shapiro that, under no circumstances, will the Connecticut State Medical Society approve any policy of his Department for reimbursing doctors of medicine that involves the principle of reduced or substandard payments for physician's services.

**Contract—Assistant To The General Manager; Employees' Fringe Benefits**

Pursuant to a previous recommendation of the Ad Hoc Committee on Staff Structure concerning the desirability of entering into contracts with members of the staff who are on salary, it was VOTED to offer Mrs. Josephine P. Lindquist the opportunity to arrange such a contract with the Society as Assistant to the General Manager, the details to be worked out with the Ad Hoc Committee on Staff Structure and be completed in time for consideration by the Committee on Budget for 1967.

It was further VOTED to request the Ad Hoc Committee to study the employee "fringe benefits" presently being provided by the Society, and to make recommendations to the Council concerning possible changes in same.

**Recommended Appointments—Board Of Examiners Of Hypertrichologists**

As required by Section 20-268, Chapter 388 of the General Statutes of Connecticut, it was VOTED to recommend to the Governor for reappointment to the Board of Examiners of Hyper-



trichologists for three-year terms the following two incumbents:

Reginald E. Gillson, Branford  
Ellwood C. Weise, Sr., Bridgeport

The present terms of these members will expire, and the new ones begin, on July 1, 1966.

**N.B.:** *The foregoing is a summary of the proceedings and actions of the Council on April 21, 1966. Detailed minutes of the meeting are on file at 160 St. Ronan Street, New Haven, for perusal by any interested member of the Society.*

**NEW MEMBERS**

**FAIRFIELD COUNTY**

Walter A. Camp, Stamford  
Armand Guigui, Ridgefield  
Martin C. Rogers, Stamford  
Herman R. Schoenwald, Darien  
Edward J. Tracey, Norwalk

**HARTFORD COUNTY**

Bruce F. Bower, Hartford  
Iain G. Campbell, Manchester  
Arthur C. DeGraff, Hartford  
Lyman B. Fogg, East Hartford  
Henry E. Gallup, Newington  
Bertram Gold, Hartford  
Benson J. Horowitz, Hartford  
George W. Hulme, Hartford  
William J. Kenny, Hartford  
William B. Laakso, Hartford  
Eugene F. Lawlor, New Britain  
Margaret Meyen, West Hartford  
Bernard Passman, East Hartford  
John W. Patterson, Hartford  
Ruben L. Shapiro, Hartford  
Manuel J. Soares, Hartford  
Yung S. Son, West Hartford

**LITCHFIELD COUNTY**

Robert S. Briggs, Torrington  
John D. Goss, Kent  
Peter Gott, Lakeville  
Ward D. Heinrich, Torrington  
Joseph McCarthy, Torrington  
Thomas, P. Millar, Torrington  
Manuel E. Mino, Winsted

**MIDDLESEX COUNTY**

Margaret O. Jones, Cromwell  
Donald E. Miller, Middletown  
Maslah Saul, Middletown

**NEW HAVEN COUNTY**

Leland S. Berger, New Haven  
George V. Cacios, New Haven  
William F. Cirimo, New Haven  
Joseph P. Dineen, West Haven  
Benjamin J. Feola, Branford  
Joseph M. Gagliardi, Seymour

Armand B. Glassman, New Haven  
Wha-Shim Han, Wallingford  
Samuel Hellman, New Haven  
Ross Jung, Derby  
David M. Kessner, New Haven  
Roland G. Martineau, New Haven  
Charles P. N. McCarthy, New Haven  
Charles W. McGuire, New Haven  
Alexander H. Pinkes, New Haven  
Krystyna I. Piotrowska-Nyerick, New Haven  
Alex A. Ritzen, Waterbury  
Donald P. Roach, Shelton  
Marshall L. Rosenbloom, Branford  
Gerard T. Scanlon, New Haven  
Sheldon S. Smiley, Derby  
Rosalie M. Starodaj, Bristol  
Pavlos D. Tjimis, New Haven  
Leon Toby, Cheshire  
Joseph G. Wihbey, Waterbury

**NEW LONDON COUNTY**

Robert W. Cranston, Norwich  
Rafael A. Cuello, Norwich  
A. John Elliot, New London  
Raymond A. Gaito, New London  
Leonard A. Greene, Norwich  
John B. Hewetson, Norwich  
Howard K. Johnson, Jr., New London  
Mary Ellen Johnson, New London  
Hans Langhammer, Norwich  
Willard J. Morse, Jr., New London

**TOLLAND COUNTY**

Robert J. Gfeller, Stafford Springs  
Thomas A. O'Boyle, Rockville

**WINDHAM COUNTY**

Fred W. Doyle, Willimantic

**1966 MEETINGS**

**September 28** — 41st Connecticut Clinical Congress to be held at Mary S. Harkness Auditorium, Yale University Medical School, New Haven, Connecticut. The program will be devoted to "Recent Advances in the Diagnosis and Management of Liver Disease" and "Recent Advances in the Diagnosis and Management of Thrombophlebitis."

**1967 MEETINGS**

**April 12-13**—Seminar on Hospital Infections in Connecticut to be sponsored jointly by the Connecticut State Medical Society, Connecticut Hospital Association, Yale University School of Medicine, the Connecticut State Department of Health and the Communicable Disease Center of the Public Health Service. No place for meeting has yet been determined.

## PLACEMENT OPPORTUNITIES

**INTERNIST** — Board certified or eligible Internist to take over fully established practice of physician who is entering Peace Corps. Located in Glastonbury, Conn., just a few minutes away from Hartford Hospital.

**PATHOLOGIST**—500 bed general, medical and surgical hospital for male Connecticut resident veterans. Salary range \$14,740 to \$19,000. Excellent fringe benefits, including group life insurance, Major Medical Insurance and Social Security. Housing accommodations available at low-cost maintenance. For further information contact: Personnel Office, Veterans Home and Hospital, Rocky Hill, Connecticut.

**DISTRICT HEALTH DIRECTOR** for Weston-Westport, Conn. Requires M.D. plus degree in Public Health or equivalent experience. Salary range \$18,500 to \$22,500, to be negotiated depending upon qualifications. Start July, 1966. Send resume to: Clifford Mills, M.D., Chairman; Weston-Westport Health District; c/o Dept. of Health; Westport, Conn. 06880.

**INTERNIST OR G.P.** for three-man group. Have regularly visiting specialist consultant staff, modern clinic facilities, scheduled training and vacation periods. Starting net income \$15,000 to \$18,000, depending upon qualifications. Partnership in one year.

**WANTED**—Locum tenens in September for general practitioner with view to permanent association.

**PEDIATRICIAN**—Third Pediatrician needed to join two other physicians presently practicing in Waterbury, Conn. Hospital facilities located nearby in this growing, industrial city.

**PEDIATRICIAN**—Another Pediatrician needed to join a multi-specialty group in New Britain. Board certification or eligibility and Connecticut license or eligibility for license required.

**ANESTHESIOLOGIST** — Board certified or eligible Anesthesiologist needed to serve in a 65 bed, fully accredited rural hospital which serves two communities of about 40,000 total population.

**OBS-GYN Associate.** Board eligible or certified. Essential that physician speak French and have completed military obligations. To assume full practice on retirement in two to three years. Located in a large, expanding Central Connecticut city.

**G.P. OR INTERNIST** wanted for full-time or part-time practice with another physician in the Stratford, Connecticut area. No investment necessary.

**G.P. OR INTERNIST** to take over practice in Greater Hartford area for cost of equipment only. Will also consider selling just equipment that is in excellent condition. Leaving practice July 1st to go into salaried position.

**MEDICAL EDUCATION DIRECTOR** — Full time Director wanted for 190-bed hospital expanding to 400 beds. Salary open. Report to Chairman, Medical Education Committee, Mount Sinai Hospital, Hartford, Connecticut 06112.

**PSYCHIATRIC RESIDENCIES**—Available in a state hospital. Comprehensive treatment facility for central Conn. area, associated with Yale University Dept. of Psychiatry and Neurology, which provides supervision in hospital and opportunities for training in areas of special interest. Senior Psychoanalyst serves as Resident Training Director. All senior administrators and Director Board certified and on faculty of Yale. Psychoanalytic training available at Western New England Psychoanalytic Institute. Personal analysis encouraged and can be arranged. Salary scale: 1st Year, \$8160 to 8800; 2nd Year, \$8400 to \$9440; 3rd Year, \$9180 to \$11,100. Many fringe benefits. Openings available at 1st, 2nd and 3rd year levels. Please send full resume with first letter to: John F. Lowney, Jr., M.D., Superintendent, Conn. Valley Hospital, Box 351, Middletown, Connecticut.

**ANYONE INTERESTED IN THE ABOVE IS ASKED TO CONTACT THE GENERAL MANAGER'S OFFICE, 160 ST. RONAN STREET, NEW HAVEN, CONNECTICUT 06511.**

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## Doctor's Office

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Larry Coletti, M.D., announces the opening of an office for the practice of general surgery at 24 Norwich Avenue, Colchester.

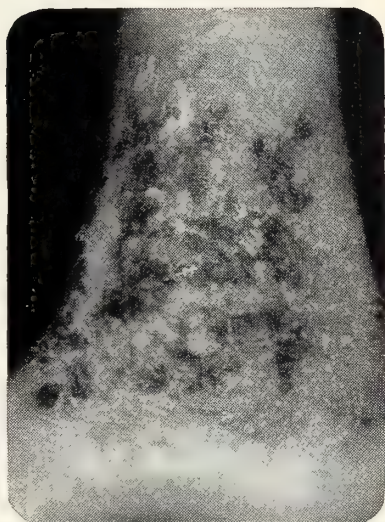
Tibor De Cholnoky, M.D., announces the opening of an office for the practice of surgery, plastic surgery and reconstructive surgery, at 1116 Summer Street, Stamford.

Matthew Owen Locks, M.D., announces the opening of an office for the practice of medicine at 153 East Avenue, Norwalk.

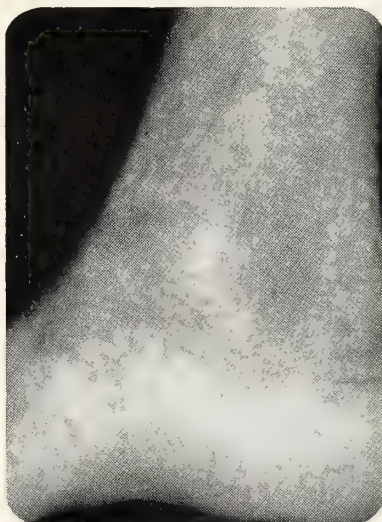
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**Contraindications:** Tuberculosis of the skin, herpes simplex, chicken pox and vaccinia.

**Precautions and Side Effects:** Do not use in the eyes or in the ear (if drum is perforated). A few individuals react unfavorably under certain conditions. If side effects are encountered, the drug should be discontinued and appropriate

measures taken. Use on infected areas should be attended with caution and observation, bearing in mind the potential spreading of infection and the advisability of discontinuing therapy and/or initiating antibacterial measures. Generalized dermatological conditions may require systemic corticosteroid therapy. Steroid therapy, although responsible for remissions of dermatoses, especially of allergic origin cannot be expected to prevent recurrence. The use over extensive body areas, with or without occlusive nonpermeable dressings, may result in systemic absorption. Appropriate precautions should be taken. When occlusive nonpermeable dressings are used, miliaria, folliculitis and pyoderma will sometimes develop. Localized atrophy and striae have been reported with the use of steroids by the occlusive technique. When occlusive nonpermeable dressings are used, the physician should be aware of the hazards of suffocation and flammability. The safety of use on pregnant patients has not been firmly established. Thus, do not use in large amounts or for long periods of time on pregnant patients.

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# MDs And The Draft

A Maine pediatrician made headlines in New England newspapers late in January. He had been called up in the draft and his appeal for a deferment had been turned down.

The situation in which that MD now finds himself — one undoubtedly shared by other physicians — might have been avoided if, upon the completion of his internship, he had applied for participation in the Armed Forces Physicians' Appointment and Residency Program. This was called the Berry Plan, named for the then Assistant Deputy Director of Defense for Medical Matters who had originated the program. An improvement in that Plan which adds 1,000 MDs is now called the Fisk Plan for the man who currently holds the post in the Department of Defense.

## Specialty Of Choice

Under this program, which has been in effect for over 11 years, physicians are selected for deferment to permit training in civilian institutions of their choice, and in the specialty of their choice. Upon completion of their residency training, they fulfill their two-year military obligation by serving in their chosen specialty in an armed forces medical facility. Depending upon the requirements of the time, members of the Fisk Plan may or may not be assigned to active duty but, if not, to the Ready Reserves.

Because of the stepped-up requirements of the Viet Nam war, no physician who completed his internship and was a Selective Service registrant in Massachusetts in 1965 escaped taking a commission either in the active or reserve forces. In August 1965, the Department of Defense held a lottery of all the accumulated requests for residency training. Men were selected in accordance with the projected requirements of the armed services and for certain specialties. Sixteen hundred young physicians for whom there were jobs were assigned to training in specialties of their choice. Another 1,000 were chosen on a contingency allowance; if the need arises for such specialists, they will be assigned to other posts.

Participation in the Berry Plan or Fisk Program in itself does not require any additional military obligation. No additional military service is available in time of peace for people in the program. MDs called to active duty will be required to serve 24 months. Those who do not serve on active duty are required to remain in the Ready Reserve for three years.

## Uncertainty Of Draft

Physicians who wait for a draft call must be prepared to enter military service at the time of the call, even though they are in practice or residency training. MDs who apply for a Reserve commission after having been ordered for induction by Selective Service will not have a choice of service, nor will they be able to select the time of their entry on active duty.

Graduates from medical schools in 1966 who do not wish to subject themselves to the uncertainty of the draft are offered, through the Berry-Fisk Program, a Reserve commission in one of the following categories: 1. active duty immediately upon completion of internship; 2. active duty as late as one year following completion of internship; and 3. deferment for residency training in specialties required by the armed services.

## A Simple Questionnaire

In May of the senior year of medical school, all graduating students who are eligible for the Berry Plan will be supplied with a brochure outlining the Plan together with a registration form. *This will be sent to the medical school address.* To participate, a physician need only answer 10 questions on an application form, mail it in and thus become eligible to participate in the competition for residency training. Upon entry on active duty, these MDs are commissioned as Captain in the Army or Air Force, or Lieutenant in the Navy.

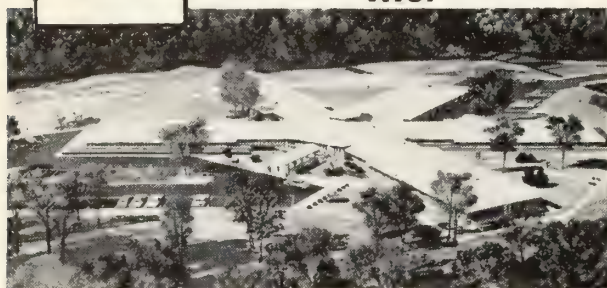
The total pay (including basic and other allowances) immediately after internship is \$866 per month for married men. One year after internship, the pay is \$893 per month for married men. Physicians trained in aviation medicine in the Army, Navy and Air Force and those trained in submarine medicine may receive extra pay of \$165 per month.

A physician is seldom so essential to a community or institution that he cannot be released to fulfill his military obligation to the country. The Berry-Fisk Plan makes it possible for every young MD to do so with the least amount of disruption to his studies and training.

*Reprinted from Massachusetts Physician, Boston, Massachusetts, Vol. XXV, No. 5, May 1966.*

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# WOMAN'S AUXILIARY

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## ANNUAL REPORT OF THE PRESIDENT — APRIL 28, 1965-APRIL 27, 1966

During its twenty-second year the Woman's Auxiliary to the Connecticut State Medical Society has taken inventory to determine its goals, the health assets and needs of its communities, its plans for the future and the education of its members.

As a first step a more permanent meeting place for its Board members was found at the Connecticut State Medical Society building in New Haven through the kind cooperation of the staff. Here the records and files of the Auxiliary are stored in an adjacent room and we have the added benefit of an adjoining kitchenette. Thus it is possible to conduct business with a minimum of distraction and a maximum of comfort. We also have the benefit of the wise council of the General Manager of the CSMS, Dr. William R. Richards and the advice and assistance of Mrs. Lindquist and her staff. In addition we have had the opportunity to establish better rapport between our Board members and the members of the Council and the staff of the Medical Society by means of a buffet luncheon and joint get-together, arranged by the New Haven County Auxiliary. This was both well attended and well received.

A concerted attempt has been made in the past twelve months to develop better liason between Auxiliary members at all levels. The president, president-elect as well as a dozen other members attended the annual meeting of the Auxiliary to the AMA in New York City in June 1965. In October the president and president-elect as well as the four Auxiliary members who represent us at the national level, attended a three day conference in Chicago designed to inform leaders of all State Auxiliaries of the goals and plans of the National Auxiliary. Later in the month the State chairmen of the committees of AMA-ERF, Community Service, Health Careers, Mental Health, Membership, Legislation, as well as the State president and president-elect were invited to a two day workshop in

New York City. The information gathered by them was passed on to county presidents and chairmen via two Board meeting-workshops and to the general membership at the semi-annual meeting and through the Connecticut Quarterly which is received by every member. In addition, the Woman's Auxiliary to the AMA has issued *Direct Line*, a newsletter for leaders, sent four times per year to State chairmen and County presidents. Six times per year all members receive *M.D.'s Wife* which includes a "Direct Line" section as well as items of interest to all doctor's wives. At the semi-annual meeting the program consisting of a presentation of "Medical Self Help" was shown and those present were urged to promote this program in their local communities. Also at the first of the "workshop" Board meetings films on safety in the home and on the road were shown and a Safety kit was distributed. There is really no reason for asking "What does the Auxiliary do?". We can inform all the doctor's wives who are not members what we try to do and how they could help by joining us.

Members of the Auxiliary have represented us at many occasions: At meetings of the Woman's Auxiliaries to the Medical Societies of Maine, Massachusetts, Rhode Island, and New York. At these the exchange of ideas is the most valuable asset.

At meetings of the Connecticut School Health Council, the Connecticut Nutrition Council, the Connecticut Health League, the newly formed Connecticut Health Careers Council, and the Board of Directors of COMPAC.

During the past year at dedication services of the Stanley H. Osborn Medical Library in the Connecticut State Health building, dedication of the New Haven Regional Center for the Retarded, and at the recent Governor's Traffic Safety Conference.

As registration aides at the symposium on Smoking in Willimantic and the Kidney symposium at Yale-New Haven Hospital.

The County Auxiliaries have raised money through various projects for Scholarship Funds and for the Student Loan Fund of the AMA-ERF. Over \$6,000 was given as direct scholarship aid to medical students, nursing students and to high school graduates continuing their studies in other health fields. \$3,375 was donated to the Student Loan Fund of AMA-ERF. We have learned that during the past year \$111,000 was borrowed by 93 medical students in our state from the Student Loan Fund.

Through the Health Careers committees in the various counties, copies of a new Health Careers Guide book were distributed in a number of high schools and received with gratitude and favorable comments by guidance counselors, one thousand reprints of a *Reader's Digest* article, "Health Careers Unlimited" and AMA Health Career kits were also given to the high schools.

The distribution of *Today's Health Guide* to high school libraries and possibly to public libraries has been promoted and is actually under way in some of the counties. This has been suggested as a joint project for the Medical Societies and their Auxiliaries—the Medical Societies providing the money at \$5.50 per copy and the Auxiliaries being the liaison officers, personally distributing the books after affixing a book plate indicating this to be a gift from the local Medical Society.

Pre-school visual screening, manning the State Medical Society's exhibits at the County Fairs, assisting in the formation of Area Health Councils and promoting legislation for additional mental health facilities were all projects of the Community Service Committees during this past year.

We have been honored to be represented by four of our members in the National "Family." Mrs. Norman Gardner has been National chairman of Rural Health and has been nominated to serve as a Director during 1966-68. Eastern Regional Chairmen have been: Mrs. Morton Arnold, Rural Health; Mrs. Edward P. Allen, Health Careers; Mrs. Dewey Katz, Community Service.

Five meetings of the Board of Directors and two meetings for the general membership, one in November and one in April, were held. At the semi-annual meeting both Dr. Orvan Hess and Dr. William R. Richards brought us up to date on the Medicare situation and the progress of the doctor draft. Also the "Medical Self-help" program was presented by a member of the State Department of Health. In April the president-elect of the Woman's Auxiliary to the American Medical Association addressed the group and explained some of the programs being planned for the coming year.

During the year we were sorrowed by the death of two members of our Auxiliary: Mrs. James Douglas Gold of Bridgeport, former president of

the Woman's Auxiliary to the Connecticut State Medical Society and Mrs. Ralph Ogden of Hartford.

The Auxiliary sincerely appreciates the guidance of the Advisory Committee of the Connecticut State Medical Society, the assistance of the General Manager, Dr. Richards, Mrs. Lindquist and her staff, Dr. Nahum of *Connecticut Medicine* and his staff. We also extend our sincere thanks to the Hartford County members who gave unstintingly of their time and effort to make the Physician's Art Exhibit such a fine success.

MRS. WILLIAM R. RICHARDS, *President*

#### PLACEMENT WANTED

**OBS-GYN** — Military obligations completed, Board eligible, with subspecialty training in gynecological cancer. Seeks opportunity for solo, partnership or association within traveling distance of New York City beginning July, 1966.

**PEDIATRICIAN** — 39 years of age, presently completing military obligations. Board eligible. Would like to associate with another Pediatrician within traveling distance of New York. Available July 1, 1966.

**GENERAL SURGEON** — 35 years of age. Board eligible, Connecticut license. Military obligations completed. Would like to join a group or form an association as of July, 1966.

**GENERAL SURGEON** — 33 years of age. Board certified in Surgery and Board eligible in Thoracic Surgery. Connecticut license, military obligations completed. Would like to practice with an associate.

**UROLOGIST** — Board eligible, Connecticut license. 34 years of age, with military obligations completed. Available July 1966 and would like to enter into an association or solo practice.

**G.P.** — 39 years of age, military obligations completed. Would like to practice with a group or an associate as of June, 1966, when he will return to this country from England.

**INTERNIST** — 34 years of age. Board eligible. Would like to form either an association or enter into a group practice either in Hartford or New Haven areas. Available shortly, upon fulfillment of exchange visitor's status from Canada.

**DERMATOLOGIST** — Board eligible, military obligations completed. Would like either to practice with a group or an associate. Available July, 1966.

**OBS-GYN** — Connecticut license. Board eligible, military obligations completed. Wishes to practice with a group or an associate. Available within one month's notice, 42 years of age, married.



## OBITUARIES

### **Joseph J. Lankin, M.D.**

**1912 - 1966**

On March 8, 1966, Dr. Joseph J. Lankin of Hartford died suddenly at Holy Cross Hospital, Fort Lauderdale, Florida, while on a golfing vacation.



A native of Pittsfield, Mass., he was Valedictorian of his class at Pittsfield High. He continued at William's College where he enjoyed a brilliant career and became a member of Phi Beta Kappa.

He distinguished himself at Harvard Medical School in both athletics and scholastically.

He interned at Hartford Hospital and followed numerous post-graduate courses at the Royal Infirmary and the British Post-Graduate School in London, England.

Dr. Lankin spent five years in the United States Medical Corp serving most of the time in the European theatre.

After his military service he became a research fellow at the Hospital for Special Surgery in New York where he trained in arthritis and rheumatology.

He established several clinics for the care and treatment of arthritic patients in the Hartford area.

He participated in numerous seminars and conferences on rheumatism throughout New England and New York. He made several appearances on television and wrote numerous articles in medical journals on his specialty.

He was an ardent golfer and won many trophies.

He was an enthusiastic baseball fan and enjoyed a short career with the Philadelphia Athletics.

He enjoyed membership in the AMA, the Connecticut State Medical Society and the Hartford County Medical Association.

He served as president of the Hartford Chapter of the Arthritic and Rheumatism Foundation. He was a devoted member of St. Joseph Cathedral Roman Catholic Church and a member of Wethersfield Golf Club.

He was highly respected in life and is deeply regretted in death.

F. C. FOOHEY, M.D.

### **Raymond T. Wise, M.D.**

**1921 - 1966**

Raymond T. Wise, M.D., 44 years old, died unexpectedly March 26, 1966 while vacationing in Nassau with wife and several colleagues. He was stricken while playing golf and died of a coronary enroute to a local hospital.



Dr. Wise was graduated from the University of Michigan and New York Medical College. He interned at St. Francis Hospital, Hartford, Connecticut and was resident physician at the New Britain General Hospital before entering practice in 1949. During World War II, he served as a lieutenant in the Navy Medical Corps.

Since 1953, he has been director of medical services at the New Britain Memorial Hospital. He was also chief of medicine at the Bradley Memorial Hospital in Southington and attending cardiologist

and internist at the New Britain General Hospital. A Fellow of the American College of Physicians and president of the Conton Honor Society of New York Medical College, he was a past president of New Britain Medical Society and a Director of the Hartford County Medical Association and the Connecticut Heart Association. He has served as medical examiner for the City of New Britain since 1963.

He leaves his wife, Mrs. Anne Karlonas Wise, three sons, Raymond T. Wise, Jr., Robert T. Wise and Philip Wise, a daughter, Miss Patricia Wise, all of New Britain; and his parents, Mr. and Mrs. Lew Wise of New York City.

ANDREW J. CANZONETTI, M.D.

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## In Memoriam

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**Blumenthal, Edward J.**—Ansonia; Long Island School of Medicine, 1932. Dr. Blumenthal practiced medicine in Ansonia for over thirty years. During World War II, he served with the United States Medical Corps, as a major with the 48th Portable Surgical Hospital in the China-Burma-Indian Theater of Operations. He was a past president of the Naugatuck Valley Medical Society and the Griffin Hospital Medical Staff. He was a member of the American Academy of General Practice, the American Medical Association, the Connecticut State Medical Society, the New Haven County Medical Association, and the Naugatuck Valley Medical Society. Dr. Blumenthal died April 24, at the age of 60.

**Leonard, John C.**—Hartford; Yale School of Medicine, 1932. Dr. Leonard was director of medical education at Hartford Hospital for 19 years. In 1944, he was the junior member of a five-doctor disaster team formed for possible World War II bombings. Dr. Leonard served at New Haven Hospital and taught at Yale before joining Hartford Hospital. He also taught at Tufts Medical College and directed the Pratt Diagnostic Hospital. Dr. Leonard was Connecticut governor of the American College of Physicians from 1951 to 1961 and had been on its board of regents since 1962. He also served as president of the Hartford Medical Society in 1964. He was a member of the Hartford Medical Society, the Hartford County Medical Association, the Connecticut State Medical Society,

and the American Medical Association. Dr. Leonard died April 26, at the age of 62.

**Platt, Irving S.**—Wolcott; University of Southern California Medical School, 1912. Dr. Platt practiced medicine in Waterbury for 46 years. He was on the staffs at the Waterbury Hospital and the Hospital of St. Mary. He was the medical examiner in Wolcott for ten years. He was a fellow of the American College of Cardiology, and a member of the American Medical Association, the Connecticut State Medical Society, and the New Haven County Medical Association. Dr. Platt died April 22, at the age of 76.

**Wellington, Harold W.**—New London; Columbia University College of Physicians and Surgeons, 1913. Dr. Wellington was the first member of Lawrence Memorial Hospital's honorary staff and head of the hospital's Orthopedic Service for 26 years. He also served as orthopedic consultant at the Coast Guard Academy Hospital. Dr. Wellington was past president of the New London County Medical Association, the Connecticut State Medical Society, and the American Medical Association. Dr. Wellington died April 18, at the age of 80.

**Sigal, Jacob B.**—Middletown; Yale University School of Medicine, 1923. Dr. Sigal was a retired attending surgeon in urology at Mt. Sinai Hospital. He was a member of the Hartford County Medical Association, the Connecticut State Medical Society, and the American Medical Association. Dr. Sigal died May 10, at the age of 69.

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## Ban On Brands—A Body Blow

There is certainly room for generic drugs. But the effort to curb the branding of all drugs would be a disastrous body blow to the public. Countless research efforts, conducted at heavy expense both in money and manpower, come to nothing. Others produce valuable but specialized drugs, needed and used by but a few people who would die without them. The successful drugs in wide use must carry the costs. There is no other way. A trade name is the producer's guarantee of quality. And it rewards research and development which mean help to sufferers from the endless ailments which plague mankind. Why put a brake on medical progress—the road to ever better health.—Editorial in *St. Louis County Medical Society Bulletin*, (32:5) February 18, 1966.



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## AROUND THE STATE

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### **New Haven County**

### **Board Of Governors**

**New Haven County Medical Association  
April 13, 1966**

The scene of the April meeting of the Board of Governors was changed to the Villa Capri in Wallingford. It was held on Wednesday, April 13, 1966.

The agenda, in the main, dealt with the agenda of the Annual Meeting of the House of Delegates on April 26th at the Statler Hilton Hotel in Hartford, and Part B of the Medicare Bill.

Dr. Stewart Petrie recommended that we establish an award to be presented at the Annual Art Exhibit of the Connecticut State Medical Society in honor of Dr. John Freiheit, a former president of the New Haven County Medical Association, and a former contributor to the Exhibit. This award will be presented this year for the first time, and then annually.

Respectfully submitted,

H. A. LEVIN, M.D.

### **Dr. Kirchner Receives Casselberry Prize**

The nation's highest award for research on disorders of the larynx has been presented to Dr. John A. Kirchner, Professor of Otolaryngology at Yale School of Medicine.

Dr. Kirchner, an authority on diseases of the ear and throat, was named 1966 recipient of the Casselberry Prize of the American Laryngological Association. The prize, last awarded in 1962, is given only when merited by exceptional contributions to the field of laryngology.

In presenting the award to Dr. Kirchner, the Association cited his originality as an investigator as well as the scientific and clinical value of his research contributions.

Dr. Kirchner's most recent research deals with the reflex nerves of the throat that protect the breathing passages from unwanted materials. His earlier work had established a close connection between the central nervous system and a small throat muscle that forms the sphincter for the upper esophagus. That research helped to explain why persons suffering from bulbar poliomyelitis and other neurological diseases find swallowing difficult or impossible.

Clinical applications of Dr. Kirchner's discoveries include improved procedures for rehabilitating persons who have undergone laryngectomy or other surgery of the throat.

Dr Kirchner joined the Yale medical faculty in 1951 as Assistant Professor of Otolaryngology and has been Chief of the Otolaryngology Section of the Yale-New Haven Hospital since 1952. He was promoted to associate professor in 1954 and to full professor in 1962.

He is President of the New England Otolaryngological Society and is active in numerous professional organizations. In 1958 he was the recipient of the Harris P. Mosher Award of the American Laryngological, Rhinological, and Otological Society, and in 1961 received a citation from the American Academy of Ophthalmology and Otolaryngology.

### **News From Yale University School Of Medicine**

New quarters for an expanded program of teaching and research in clinical medicine at the Yale-New Haven Medical Center were dedicated on May 10.

Housed in the recently completed fifth and sixth floors of the Hunter Building on Davenport Avenue are the *Lawrence M. Gelb Foundation Clinical Research Unit*, devoted to the study and treatment of specific diseases in selected patients, and the *Clinical Research Training Center*, where young physicians are given intensive instruction in the methods used to investigate disease.

The new 14-bed clinical research unit is an extension of the Medical Center's clinical research program established in 1960 under a grant from the National Institutes of Health to enable physicians to investigate unusually complex or obscure disorders occurring in patients. Similar units devoted to clinical research in pediatrics and pharmacology — with six and eight beds, respectively — have been functioning in other buildings of the Medical Center since the inception of the program.

The opening of the new unit brings to a total of 28 the number of beds reserved for patients whose medical problems fall within the framework of a specific research project. These patients are referred by other divisions and clinics of the Medical Center and, as participants in the clinical research program, they pay no fees. Operating costs of the

program are underwritten by the NIH and all physicians conducting studies under the program are members of the faculty of the Yale School of Medicine.

Occupying the fifth floor of the Hunter Building, the Lawrence M. Gelb Foundation Clinical Research Center is directed by Dr. J. William Hollingsworth, Associate Professor of Medicine at Yale. Ailments under study in the unit include chronic kidney infections, diseases of the heart and lungs, and skin disorders related to diet. In addition to patient rooms, the unit includes conference rooms, a lounge, and a special-diet kitchen.

This program, also supported by the National Institutes of Health, has been operating on a pilot basis since 1963. With the addition of the new laboratory facilities in the Hunter building, it will move into high gear this July when several selected physicians who will have just completed their internships will begin an intensive course of study in investigative medicine.

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The W. K. Kellogg Foundation of Battle Creek, Mich., has awarded \$153,150 to Yale University to expand its program in education for hospital administration.

The expanded Program in Hospital Administration at Yale will increase the length of graduate study on campus from two semesters to three semesters and a summer. During the additional time more basic content will be provided in Industrial Administration. The length of administrative residency in a hospital will be pared from eleven to five months, and the essay required for a Master of Public Health degree will be written under closer supervision of the faculty.

A postgraduate fellowship is also featured in the revised program. Its purpose is to bring a practitioner into the program annually to act as a "teacher-student"; he will stress his own experience, conduct classes covering new developments, and do independent studies under a faculty member's guidance.

Since the Kellogg Foundation grant in 1947 subsidized the program's establishment at Yale, more than 150 students have received their master's degrees for study of hospital administration. They are now at work in many parts of the world, including Samoa, Iran, the Philippines, Canada, South America and Liberia. Classes taking the course annually average 11 or 12 students.

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Dr. David Seligson, professor of medicine and pathology at Yale and director of clinical laboratories and school of medical technology at Yale-New Haven Hospital, was selected to receive the John

Gunther Reinhold Award of the Philadelphia section of the American Association of Clinical Chemists.

The presentation was made at the chapter's dinner last month in Philadelphia.

Dr. Seligson directs the Clinical Chemistry Laboratories for Yale-New Haven Community Hospital.

John Gunther Reinhold, Ph.D., for whom the annual award is named, is professor and chairman of the Department of Biochemistry at the American University, Beirut, Lebanon.

Prior to his arrival at Yale, he was director of the division of biochemistry, Graduate Hospital of the University of Pennsylvania for five and a half years.

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Dr. Vernon W. Lippard, Dean of the Yale School of Medicine since 1952, has asked that he not be considered a candidate for reappointment when his third five-year term expires in June, 1967.

Dr. Lippard, who will be 62 next year, now holds the country's record term of service, 20 years, as a medical school dean. Prior to assuming his present post at Yale, he had held the medical deanships of the University of Virginia, from 1949 to 1952, and Louisiana State University, from 1946 to 1949.

A statement issued by President Brewster today said: "Yale has been lucky to have the leadership of Dean Lippard during the crucial mid-century decades of its medical development. New Haven as well as the University owes a great debt to Dean Lippard for the progress of Yale-New Haven medicine over the last fifteen years. Our medical science, medical training, and medical care are all a source of pride to both the university and the community. We are resolved to maintain our pace along the road the Dean has marked out for us. It is most fortunate that we will continue to have Dr. Lippard's advice and counsel in this effort."

### **Connecticut Mental Health Center Dedication**

The Connecticut Mental Health Center will dedicate its new building on 34 Park Street in New Haven, on Friday, 30 September, and Saturday, 1 October, 1966. The Connecticut Mental Health Center is a collaborative venture of the State and Yale with Dr. F. C. Redlich, Chairman of the Department of Psychiatry at Yale, serving as Director.

Dedication ceremonies will include talks by Governor of Connecticut John Dempsey, Yale President Kingman Brewster, New Haven's Mayor Richard C. Lee, Commissioner of Mental Health Wilfred Bloomberg, M.D., and Chairman of the Board of Mental Health John Donnelly, M.D.

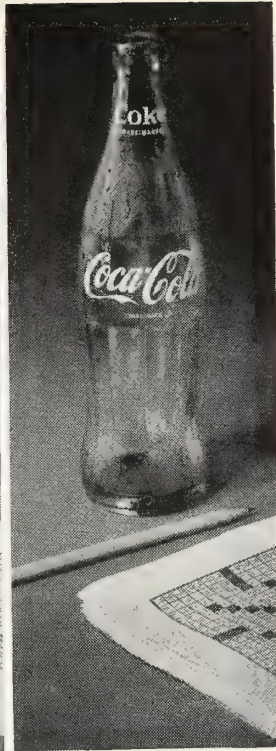




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11:53 pm



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## NEW BOOKS IN REVIEW

**THE BODY.** By Alan E. Nourse and The Editors of *Life*. Sixth volume in the Life Science Library series. Time Publishers, New York, 1964. 200 pp., illustrated, 72 pages in full color. \$3.95.

Reviewed by: LOUIS H. NAHUM

The Body, latest edition in the Life Science Library series, explores in text and illustrations the countless functions and abilities of the human body.

Dr. Alan E. Nourse begins with a discussion of some of the body's most important features, then describes in a pictorial essay man's increasing knowledge of it, from Cro-Magnon man's "surgery" to sometimes fanciful medieval concepts to the first detailed drawings of the anatomy by the Flemish-born Andreas Vesalius.

In the book's eight chapters, Dr. Nourse describes the body's components. Each chapter is supplemented by a graphic pictorial essay which complements the chapter it follows, illustrating the subject in depth or adding to the information already supplied.

This book makes comprehensible to the lay public how the form and function of the human body mold to produce a body of great efficiency and almost incredible flexibility. It is an excellent book for the intelligent layman and all paramedical personnel.

**PHYSICAL EXAMINATION OF THE SURGICAL PATIENT.** By J. Englebert Dunphy, M.D., F.A.C.S. and Thomas W. Botsford, M.D., F.A.C.S. W. B. Saunders Company, Philadelphia, 1964, 396 pp., 215 figures, 1 color plate, \$8.50.

Reviewed by: DAVID M. LITTLE, JR.

This is the third edition of a small volume on physical diagnosis that is by way of becoming a classic in its field. It is intended primarily for the medical student, but it will be read with profit by any doctor who has not retired to an administrative office or a research laboratory—in short, any physician who is still engaged in the treatment of patients. Furthermore, although the authors are surgeons and they are concerned with the examination of patients from the surgical point of view, physical diagnosis remains physical diagnosis no matter what the particular specialty of the examining physician may be; and the methods of observation, of palpation, of examination of external structures and internal viscera, and of deduction described in this book will be equally as valuable to an internist, or a neurologist, or an ophthalmologist, as to a surgeon.

The book is logically divided into two sections, the first part being devoted to the elective examination and the second part to the emergency examination. There are a few pages on generalities and history taking at the beginning of the first section, and then separate chapters devoted to physical examination of each region of the body. Particularly outstanding are the long chapter concerning the examination

of the abdomen (which should perhaps not be surprising in view of the careers of the authors), the subsequent chapter on the examination of the abdomens of infants and children and the chapter on the examination of the surgical cardiac contributed by Dr. Albert Starr.

The second section of the book, concerning the emergency examination, begins with a short discussion of resuscitative procedures, contributed by Dr. Leroy D. Vandam, and the immediate treatment and examination of the injured patient. Then, as in the first section of the book, there follow separate chapters devoted to examination of the injured patient according to regions of the body: injuries of the head and face; injuries of the thoracic wall, heart and lungs; abdominal injuries; injuries of the kidney, bladder and urethra (fractured pelvis); and injuries of the spine and extremities. The final chapter in this second section concerns the emergency examination and mapping the extent of burns.

The style of writing is simple, lucid and smooth flowing, and the generous use of line drawings (which are extremely well done) and photographs add greatly to the meaning of the text. There is an appendix which is a check list for the physical examination, a bibliography of about seventy-five selected titles, and a comprehensive index. The printing, paper and binding are what one has come to expect of a good publishing house such as Saunders.

This is not a textbook of surgery; it is a book of technique and procedure. There are no long descriptions of diseases, but enough pathophysiology is included to give meaning to the physical signs and the methods of examination. This will be a book of particular value to the medical student and house officer; but as already noted above, it will be of assistance in the examination of any patient by any physician.

**JAMA SELECTED QUESTIONS AND ANSWERS.** Selected from the 1965 issues of the Journal of the American Medical Association. Foreword by Alfred Soffer, M.D., Editor, Questions and Answers Dept., Journal of the American Medical Assoc. \$2.50 each in U.S., U.S. Possessions, Mexico and Canada; \$1.50 each for Medical Students, Hospital Interns and Residents and \$3.00 each in all other countries.

Reviewed by: LOUIS H. NAHUM

The Editor of this book is in direct and constant communication with the practicing physician. In this way he has identified the topics of current concern. Here we find published inquiries and the consultant's comments. It forms a real type of post-graduate education.

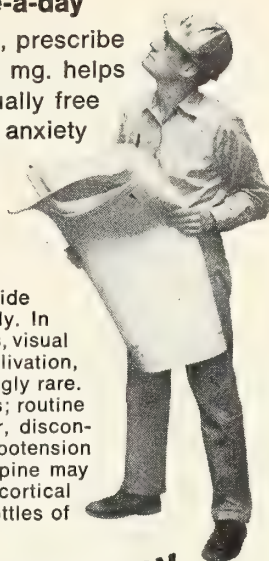
Sometimes two consultants give their answers, not always in agreement. Such discussions provide valuable references for practice, teaching and not infrequently clinical investigation. Every physician should own this book and use it daily. It is valuable and pertinent to the requirements of everyday practice.



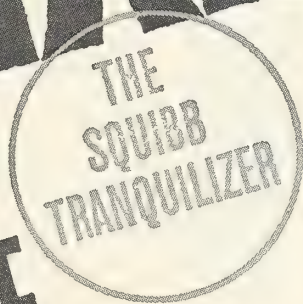
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### Artificial Heart Valves Questioned

Two prominent surgeons have called for a hard second look at the use of artificial heart valves.

While acknowledging the value of artificial valves in extreme cases, they say that the valves have been overused.

Sir Russell Brock, president of the Royal College of Surgeons, advocates more use of heart valves transplanted from cadavers. It may even be possible to transplant heart valves from other animals, he suggested.

Charles P. Bailey, M.D., director of thoracic and cardiovascular surgery at St. Barnabas Hospital, New York City, has led research in repairing existing heart valves with other tissue from the patient's body. This may prove more successful than artificial valves, he said.

The two surgeons' comments appears in the Medical News section of the current Journal of the American Medical Association. They spoke at a symposium on rheumatic and coronary heart disease sponsored by St. Barnabas Hospital.

Artificial heart valves haven't been in use long enough to evaluate their long-term survival rate, Dr. Bailey said. Nevertheless, failure rates as high as 37 per cent within 12 months after implantation have been reported.

Valve-repair techniques at least equal the survival rate of artificial heart valves, and should be expected to surpass it, Dr. Bailey said.

"Obviously, when a patient has no future without an operation, valve (removal) is not only justifiable, but can be a brilliant, worthy and highly commendable form of treatment," Sir Russell said. "There is, however, much evidence that the limitations of valve (removal) and replacement are often totally ignored."

Sir Russell's principal objection to the artificial valve is that it represents too radical a departure from the shape of the natural valve. He questions whether an artificial valve will be long tolerated by the body.

Improvements in cadaver-valve transplantation techniques have produced excellent results with low death rates," he said.

At Guy's Hospital in London, where Sir Russell is director of cardiology, the aortic valves of more than 100 patients have been replaced with valves from cadavers. The earliest of these patients has now survived 3½ years.

While agreeing that the artificial valve has limited use, Dr. Bailey differed somewhat on alter-

native procedures. He favors reconstructing the original valve with other tissue from the patient's body.

There have been complications in replacing sections of artery with sections from cadavers, and these complications probably apply to the more difficult task of heart-valve replacement, he said.

In addition, it is difficult to obtain an adequate supply of cadaver heart valves, Dr. Bailey said.

Sir Russell agreed that supplying a variety of heart valve sizes from cadavers is difficult.

"The solution may lie in the use of hetergraft valves, from other animals), and we should not turn lightly from developing their wide use unless, it is shown that they are not satisfactory on immunological grounds," he said.

With further experience, the need for artificial heart valves may be reduced to only occasional aged and terminally ill younger patients, Dr. Bailey said.

The great wave of enthusiasm for artificial heart valves in recent years should not blind the surgeon to the fact that it is, in reality, a great human experiment, Sir Russell warned.

"It can be argued very reasonably that it is an investigation that has to be made, an experiment that has to be tried. This is entirely justifiable if we remember that it is an experiment, a deliberate, widespread human experiment," he said.

### Is The Autopsy Out Of Date?

The autopsy, once a major part of medical teaching and investigation, has fallen on hard times.

Thousands of autopsies are performed every year, but they no longer occupy the central place in medicine that they once did.

There are a number of reasons, including the development of laboratory methods for diagnosing disease, the shortage of pathologists' time, and a general shift in emphasis in medical teaching and research.

Few, if any, physicians would want to eliminate autopsies entirely, but many medical authorities are questioning the need for the number that are performed.

Is the postmortem examination thus an outworn relic from the past? No, indeed, say five pathologists and a clinician in the current Journal of the American Medical Association. However, they offer several suggestions for improving the autopsy.

During life, the patient is studied with the latest, most up-to-date medical procedures, points out Joseph F. A. McManus, M.D., of the Department of

Pathology, Indiana University School of Medicine, Bloomington. If the patient dies, however, the autopsy, is frequently a superficial procedure that has been unchanged for a half century or more.

Two changes could improve the autopsy, points out a *Journal* editorial. The first is to restore the careful, detailed investigation that helps make it a research procedure. This may mean reducing the number of autopsies.

The second needed change is to "restore the autopsy to its rightful place as teaching instrument," the editorial said.

"Through autopsies the pathologist can answer various specific questions and provide simple 'factual' data important for the physician, the patient's family, and the statistician. For example, did the patient have peritonitis following an operation? Was a sudden death due to an embolism? Was a lung tumor primary or metastatic? Answers to such questions do not constitute 'science,' they do not advance conceptual or general knowledge, but they help the overall care of patients."

The autopsy is uniquely suited to study an individual disease, said Milton G. Bohrod, M.D., of the Department of Pathology, Rochester, N.Y., General Hospital.

"Every death corresponds to a failure, either of the individual physician, or, more commonly, of medicine as a whole. Every necropsy (autopsy) represents a last attempt to solve the enigma of the individual illness," he said.

Autopsies on all deaths probably should be done in teaching and clinical research centers, said Sidney C. Madden, M.D., of the Department of Pathology, School of Medicine, University of California, Los Angeles. This ideal cannot be reached in non-teaching hospitals, he said. The goal then must be selection of cases which yield the most useful information.

"Finally, the question can be asked, who is going to do autopsies?" said Charles S. Davidson, M.D., of the Thorndike Memorial Laboratory, Boston City Hospital, Boston, Mass. "Many pathologists nowadays have really become molecular biologists and are no longer interested in the autopsy and in pathologic anatomy.

"In conclusion, I am sure that we cannot give up the autopsy," he said. "It is absolutely necessary, but it must seek its place among all the various methods of study of the patient, of groups of patients, in teaching, or in medical research."

Other symposium participants were J. Beach Howard, M.D., of the Department of Pathology, Cleveland Clinic, Cleveland, Ohio, and Alfred Angrist, M.D., of the Department of Pathology, Albert Einstein College of Medicine, New York City.

## Multiple Sclerosis Clusters Found

There appears to me an unidentified environmental factor distributed in much the same way as the clusters of multiple sclerosis found in various countries, says an article in a current publication of the American Medical Association.

Identifying this factor may give a clue to the cause of multiple sclerosis (MS), one of the most common primary diseases of the nervous system.

The unknown factor seems to indicate, the author said, that MS is an "acquired exogenous" disease—meaning one acquired from elements outside the body.

"It would be significant to be able to say that MS is an acquired disease," said an editorial in the current *Journal of the American Medical Association*. "If this concept and the consequent inferences are tenable, a valuable tool in work with the disease may exist."

Up to now, the illness has generally been considered of unknown cause, unpredictable course, and unresponsive to therapy.

The author, J. F. Kurtzke, M.D., summarizes recent studies of the incidence of multiple sclerosis. His report appears in the February issue of the *Archives of Neurology*. Dr. Kurtzke is a staff member of the Veterans Administration Hospital and the Georgetown University School of Medicine, Washington, D.C.

Multiple Sclerosis incidence varies in wide bands across the earth, he noted. The northern United States, Southern Canada, and northern Europe are in the highest-frequency band (30 to 60 cases of MS per 100,000) include the southern U.S. southern Europe, and Australia. Asia and Africa seem to have the lowest incidence of MS. These figures may be distorted by a lack of adequate surveys in some areas.

More important, Dr. Kurtzke noted that in almost every North European country where MS has been surveyed, the disease appears in clustered areas.

Dr. Kurtzke concludes that these clusters indicate the presence of an exogenous, or outside, factor associated with the disease. He does not speculate what this factor might be, but does eliminate some possibilities.

Climate or diet seem to be ruled out. The cluster areas of disease are too small to be affected by these, he said.

Heredity may not be a factor, either. In Denmark and Switzerland, where two generations of patients were surveyed, MS could not be attributed to familial cases. Neither could it be correlated with the distribution of doctors or medical facilities.





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A National Conference on Infant Mortality is being sponsored by the American Medical Association's Committee on Maternal and Child Care. The Conference will be held on August 12-13, 1966, at the Fairmont Hotel in San Francisco, California.

An open invitation to attend is being extended to chairmen and members of all state and county Maternal and Child Care; Perinatal and Maternal Mortality Committees; State Health Department Directors of Maternal and Child Health; medical school faculty members in Departments of Obstetrics and Gynecology, Pediatrics, and Preventive Medicine.

The program has been planned to explore effective approaches for continuing the reduction of infant mortality. Special workshops will be arranged to discuss the identification of high risks, organization and delivery of special care services, manpower utilization, continuity of reproductive care and problems of prematurity. Other subjects to be cov-

ered by special speakers will include perinatal mortality studies, obstetric and pediatric education programs, research questions, expectant parent and sex education, and population control.

Those interested in receiving further information about registration for the Conference should write the Secretary, Committee on Maternal and Child Care, American Medical Association, 535 North Dearborn Street, Chicago, Illinois 60610.

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### Drug Revolution In Psychotherapy

Following a decade of wide clinical use, psychotherapeutic drugs are firmly established as potent and useful therapeutic agents. These drugs have sparked a revolution in the treatment of major emotional disorders, such as schizophrenia. This tremendously disabling illness, which strikes at an early age and may last a lifetime, is becoming more amenable to treatment. Hospital treatment of the insane, only recently a national disgrace, has now become more humane, more energetic, and, most of all, more effective, due largely to drug therapy. —Leo E. Hollister, M.D. in *Clinical Pharmacology and Therapeutics*, (6:417), July-August, 1965.

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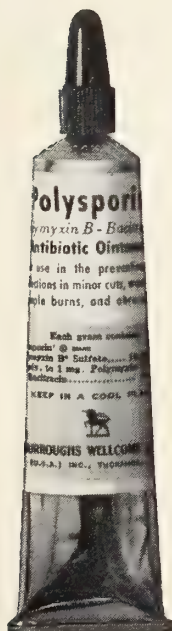
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*JAMA Selected Questions and Answers.* Foreword by Alfred Soffer, M.D., Editor, Questions and Answers Department, Journal of the American Medical Association. Selected from the 1965 issues of J.A.M.A. Price: \$2.50 each in U.S., U.S. Possessions, Mexico and Canada; \$1.50 each for Medical Students, Hospital Interns and Residents in U.S., U.S. Possessions, Mexico and Canada; and \$3.00 each in all other countries.

*Synopsis Of Obstetrics.* Seventh Edition. Charles E. McLennan, M.D. The C. V. Mosby Co., St. Louis, Missouri, 1966. 471 pp. with 166 illustrations including 4 in color. \$6.85.

*Horizons Unlimited.* A Handbook Describing Rewarding Career Opportunities in Medicine and Allied Fields. American Medical Association, 1966. Program Services Department. 134 pp.

*United States Army In World War II.* The Technical Services. The Medical Department: Medical Service in the Mediterranean and Minor Theaters by Charles M. Wiltse. Office of the Chief of Military History, Department of the Army, Washington, D.C., 1965. 664 pp.

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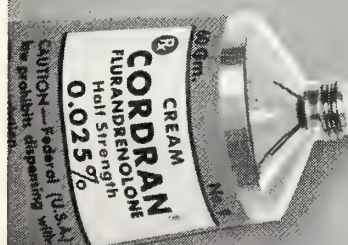
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# Connecticut Medicine

## editorials

### Cancer Chemotherapy

In 1948 Farber<sup>1</sup> and his colleagues first reported the effect of aminopterin on acute leukemias in childhood. This opened possibilities in the treatment of advanced malignancy previously reserved only for a small group of late tumors amenable to whole body radiation. Many other toxic agents were soon to follow and treatment could now be offered to the patients dying of hopelessly widespread disease. Such treatment at first was offered with the expressed hope of slowing the growth of widespread tumors or possibly even producing its regression. In the mesenchymal tumors of the blood forming organs such as the lymphomas and leukemia, and in certain other tumors of childhood (Wilmsrhabdomyosarcoma) the benefits to be attained from drug therapy are quite impressive, in terms of long-term remissions and even some that might at times be termed cures.<sup>2</sup>

In epithelial cancers of the adult, the best results achieved to date have been short periods of stability or regression of the tumor. It is therefore in this group that the most pressing problems present themselves on the use of cytotoxic drugs. Moore<sup>2</sup> has detailed these problems under three headings: clinical investigation, host resistance, and treatment policies on late cancer. As to clinical investigation, he points out how difficult it is to achieve intelligent clinical research. One can only try one drug in one person and relief in many patients is rare. If other modalities are needed in the interest of the patient, these cloud the result. Furthermore, there are few discriminating chemical indices that can be used to gauge the progress of the treatment.

As it is now we know nothing of the result of the drug until weeks have passed. There are only a handful of chemical criteria for the short term evaluation of drug action in cancer. These include measurements of the alkaline phosphatase in liver metastasis, acid phosphatase in prostatic carcinoma that has invaded bone, lactic dehydrogenase (LDH) in a few widespread tumors, urinary calcium in skeletal involvement. Then one can detect excretory products of a relatively few secreting tumors such as gonadotrophins in choriocarcinoma, pressor amines in pheochromocytoma, corticosteroids in adrenal carcinoma and indolacetic acid in carcinoids. Beyond these few measures we really have nothing to rely on except weeks or months of clinical observation. The patients are either better or worse, alive or dead. In short clinical investigation is extremely difficult.

From experiments on tumor transplants and our growing knowledge of host resistance there has developed a distinct possibility that the same agent we are using in chemotherapy may be dampening some mitotic activity in the tumor, while at the same time it is lowering the patients resistance to the tumor. These two simultaneous actions can explain some of the baffling phenomena seen in treated patients who seem one day to be better and another week far worse. The drug is inhibiting mitotic activity and antibody synthesis simultaneously. To study this double action, an investigator needs not only the chemical indices of tumor growth previously mentioned but also better methods for measuring the concentration of the drug in the blood and its excretion in the urine and for immunologic studies in cancer.

## THE COVER

### RHAZES AND ARABIC MEDICINE

THE WEST is deeply indebted to medieval Arabs for preservation of ancient Greco-Roman knowledge during the Middle Ages, and for improving on it. Our numeral system and many words, such as alcohol, came from the East, as did many medical advances. Leaders in Arabic medicine were the Persians, Rhazes and Avicenna. Rhazes (865-925 A.D.), noted for keen observation and inventiveness, was first to describe measles and smallpox; to observe pupillary reaction to light; to use mercurial purgatives; and to publish a text on children's diseases. His teachings were very highly regarded for many centuries.

Under "treatment policy" in the patient with late cancer, Moore points out that such problems first arise when the patient first learns that he has a recurrent tumor. The former tendency to "shop around" among institutions seeking the "latest treatment" has been abated by the use of chemotherapy. Many patients now retain confidence in their institutions and their doctor because chemotherapy is available to them in their extremity. The cytotoxic agents have saved thousands of patients from being subjected to multiple small doses of creatine (Krebiozen). With chemotherapy the patient achieves the belief that something newly discovered is being used to help him. He believes that relief might be forthcoming and occasionally it actually is. If the drug is used in doses which avoid systemic toxicity (this is not always achieved) the early use of these drugs during a recurrent phase of malignancy is justified both on psychological and medical grounds and is strongly urged even if the patient is asymptomatic.

The problems of treatment policy become much more difficult when the patient gets sicker. Then the drug must be used in toxic concentrations or not at all. If used the patients undergo bone marrow depression, susceptibility to infection and destruction of gastro-intestinal mucosa with resulting massive hemorrhage. These complications have given rise to a popular notion that doctors have become too meddlesome in treating late cancer and that the doctor is preventing the patient from dying with "dignity." The patient is pictured as succumbing finally in a tangle of tracheotomy tubes, positive pressure breathing apparatus, intravenous infusions, blood transfusions after cancer chemotherapy.

The actual facts of medical treatment in late malignancy are far removed from this dismal image. In most hospitals and in the hands of sophisticated physicians and surgeons therapy in widespread cancer is neither ill advised nor meddlesome. Some patients actually can be rehabilitated by a variety of means. There is a considerate withholding of desperate treatment usually with the knowledge of the family and with watchful waiting and the use of appropriate analgesics in the last days of the patient. Actually the withholding of such cytotoxic drugs demands as much discrimination as giving them.

Every consultant has seen patients to whom withholding of treatment has brought much unnecessary misery. In the last weeks of a patient's life it is a challenge to the clinical judgment and entire facility of a modern hospital to use chemotherapy intelligently. There appears to be a final point in the progress of cancer of the colon, stom-

ach, thyroid, breast, pancreas, and biliary tract beyond which the use of cancer chemotherapy rarely if ever yields a remission. At this point it is only an emotional prop for the patient and his family. But it becomes an immensely complicating factor particularly through damage to the gastro intestinal mucosa. Of course it is the doctor's job to be able to discern when this moment has arrived.

When all has been said and done, there is an optimistic side also. The use of these drugs as continuous infusions or localized pump-oxygenator infusions, their use with systemic antagonists and their combined use with radiotherapy and surgery represent important new sources of hope for the patient with late malignancy. They certainly deserve further intensive study.

L.H.N.

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## Ethical Problems In Human Experimentation: 2. In Relation To Medicine

The physician devoted to extending the horizons of his art which can be done only by observation and experiment, is and rarely needs to be held back from rash ventures. Hippocrates enjoined us first to do no harm. Here is obviously a dilemma: to learn how to increase our capacity for cure and at the same time take no risks that may be in the best interest of the individual subject. But medical relations have become more complex in an age of rapid advances, more radical therapy, bolder techniques, specialized roles within the medical profession and collaboration with other scientific disciplines.<sup>1</sup>

Experimentation goes on in a wide spectrum of activity. The earlier court decisions did not reflect this situation because they held that a physician experiments at his own peril.<sup>2</sup> However these statements refer to a doctor's departure from an accepted mode of treatment. But it is true today that experimentation involves a whole range of practices. One is the practice of therapy when there is no generally accepted mode of treatment as for example chemotherapy for certain kinds of cancer. Then there is the use of drugs or injections on patients not for immediate therapy at all but for the sake of observations of the results with a view





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to the eventual improved treatment of sufferers who may or may not include the particular patient. Finally at the other end of the spectrum is this use of non-patients for experimental subjects. What are the safeguards against abuse?

One is the doctor-patient relationship. In dealing with a patient the doctor is guided by his dominant treatment aim and responsibility. His role is relatively uncomplicated although the decisions may be difficult enough to reach. He is guided by the welfare of the patient whether to disclose and how fully the nature and the risks of the treatment. To the doctor the patient is considered an end not a means. This factor, the immediate welfare of the individual, is the doctor's inner check.

As one moves away from the doctor-patient relationship other safeguards, Freund points out, than the inner check become more crucial. One is disclosure and consent. Another safeguard is the external check of another echelon of medical approval. Still another safeguard might be a requirement that all the results of the experiment be submitted for publication when they are negative or not, as a check on an overly optimistic exuberant, or ambitious experimenter.

There are all kinds of problems about subjecting a patient to the legalism and the tension of signing a document after disclosing what the doctor wishes to do. The document may seem horrendous to the patient in his condition. Of course explanation and consent are not required if the new technique is strictly necessary for treatment. This is especially true if the risk is not undue and if in the judgment of the physician and a higher echelon of medical advice agrees that it is for the well-being of the patient.

When we reach the case of the non-patient and of the normal subject we enter ground covered by the Nuremberg code gotten up by a committee of the American Medical Association. It demands that voluntary consent of the human subject is absolutely essential. Freund sees a number of difficulties even with this blanket requirement of full disclosure and consent. There is the blind or double blind experiments in which non-disclosure is deemed essential to the design of the test. In such a case there is the greater need for an external check through the approval of a higher echelon. But even in such a case the risk involved should be relatively light. We are here dealing in other words with a number of variables. The degree of risk, approval of the experiment and degree of disclosure and consent.

There are other problems too. What about the subject who does not possess full capacity to consent, in particular the problem of children. Here

the rule is that parents may consent for the child if invasion of the child's body is for the child's benefit or welfare. This is true even if the benefit is psychic welfare such as has become celebrated in the question of one child donating a kidney to a sibling. But what of the donor to a stranger when benefit to the child is not present. It may then be that children should be ineligible when the risk is relatively slight.

Then there is the question of giving payment as it may affect the reality of the consent. Freund suggests that the amount paid should not be so large as to constitute undue influence, this so large as to obscure the appreciation of risk and weaken the will to self-preservation. "We ought not be put in the business of buying lives."

Then there is the problem of students who are of age. Here Freund suggests that since they are in some respects under the tutelage of the university, in addition to the students consent, it should also be given by authorities of the university also. As is now required at the Harvard Medical School where both the administrative board and the Department of Environmental Health must give approval for the employment of students as volunteer subjects.

The problem of consent is especially delicate in the case of prisoners with whom an assurance of parole or commutation of sentence would constitute undue influence or duress through promise of reward. Freund insists there should not be a pressure to conform within the prison generated by the pattern of rejecting parole applications of those who do not participate. It should not be made informally a condition of parole that one go along, be a good prisoner, and subject himself to mild experimentation.

Freund's final peroration is worth quoting in full. "In closing let me say that to me medicine and law and art have an essential affinity. As the artist finds his freedom in the constraint of his medium, in the canons of taste and in respect for the limitations of his material, so the judge and the physician too find their freedom in their fetters, in the symbolic codes that assign them their roles and render it tolerable to make judgments involving life and death—fetters that somehow make it possible to surmount the agony and the absurdity of human decisions."

L.H.N.

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## Utilization Committee Or Medical Audit

For the past few months a prime subject of discussion in hospitals has been the implications of the Medicare act for the future of American hospitals and medical practice. For the present much of the impact is entirely a matter of conjecture. One however has caused consternation and dismay among many hospitals and their medical staff. The Medicare act does require that every hospital and extended care facility that wishes to qualify as a provider of services must have a utilization review plan and that it must have two mechanisms. One is the medical necessity for inpatient services during a continuous period of extended duration. The second is retrospective, and requires a review of admissions, the duration of stay and the necessity of the professional services furnished including drugs, biologicals, the use of facilities, services. It is this part which may be called utilization evaluation.

These two problems, necessity for admission and efficient use of the facility will probably be found best handled by two separate committees. The method the committees will use to deal with them will vary somewhat from one institution to another and is spelled out by Slee.<sup>1</sup> The medical necessity determination is rather new to most hospitals although some admission and discharge committees and a few utilization committees have worked on this problem. The utilization evaluation is not new. Appropriate use of hospital and medical resources and facilities has always been of concern to conscientious and thoughtful physicians and hospital administrators.

Wherever there was a "medical audit" it has always pointed out excessive use of drugs, unnecessary hospital stays, overburdening of the laboratory with recurrent routine "batteries" of tests and other wasteful practices. It should here be emphasized that the medical audit did not have its origin from attention to the conservation of resources. Rather, it sprang from a need we all feel and pursue—the drive to promote the best possible care.

We owe to the American College of Surgeons and the American College of Physicians the leadership in developing methods for monitoring the quality of medical care through standards their diplomates must achieve. However, their diplomates form the core of hospital staffs and it is not surprising that the hospital medical staffs should develop a methodical approach to monitoring the quality of care and maintaining the highest medical standards. This began with a few hospitals and the American College of Surgeons, first by estab-

lishing the professional activity study and proceeded to the development of the medical audit program.

A medical audit is defined as the evaluation of the quality of medical care as reflected in the medical record. The word quality holds the key. In a medical audit quality can be defined as the degree of conformity with accepted principles and practices. These desired standards of excellence obviously require certain fundamental things be done for every patient. It means that the correct steps and procedures be taken for specific types of patients and that investigation, diagnosis and treatment be tailored to the individual patient. As Slee states "the goal is to achieve those standards which each physician would like to have met when he or a member of his family is the patient and which he sincerely tries to maintain in his own practice."

The scope of the medical audit is comprehensive for it is just as concerned that our medical and hospital resources be conserved as is the utilization committee. However, in addition, equal attention is given to the question of whether every patient gets what he needs for his particular problem. The medical staff which is conducting an internal medical audit is also carrying out a utilization evaluation as well although this aspect is only a portion of the medical audit's total function.

The second portion and probably the more important one, is the medical audit as being a powerful tool to keep physicians abreast of medical progress and to prevent professional obsolescence. When it was first introduced its aim was to reinforce the education arm of medicine so that the fruits of research are transmitted to the clinician and translated into practice. The medical staffs own review of its daily hospital practice is an important technique for keeping up to date. It helps us to discard old practices, adopt new ones, and to make the best use of available resources, whether they be hospital beds, tests, drugs or personnel.

Slee describes the methods generally employed in medical audit. A two or three man subcommittee on each of the major hospital services is formed which can discuss the topics falling within its jurisdiction. Both general practitioners and specialists participate since the goal is education and not the judgment of the general practitioner by the specialist. The review is not of the physician but of medical practice.

The process is progressive and usually goes through two screening steps, and then by examination of selected individual case records. The first is a review of descriptive statistics which show the kind of patients, their diagnosis, the operation performed or treatment carried out, the use of blood,





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length of stay, complications, consultations, death rates, etc.

Then follow a review of detailed statistics of groups of patients in order to see how specific aspects of care correspond with what the best care would look like. Only then can examination of individual cases be undertaken especially if the statistics turn out to be at variance with expected standards. Obviously if the care of the patients is to be audited, it is essential for the hospital to have a medical record information retrieval system to give essential statistical data. There must be progress detail permitting each statistic to be converted into the case histories of individual patients. There will need to be adequate original records, modern methods of tabulation, presentation and analysis of data, skilled information retrieval personnel in the medical records department ready to help the medical staff.

There will have to be a medical staff trained in the technique of medical audit. At the present time this is not taught in medical schools or residencies. Clearly there are two aspects to this process: development of criteria against which the case will be matched; working with information in statistical and coded form in order to screen large numbers of cases rapidly, looking for possible problem areas.

Criteria will be derived from the committee's own knowledge of what constitutes good practice, a search of the literature and consultation with specialists when doubts may arise. This type of thing is found in handbooks of therapy often gotten out by individual departments, but has to be interpreted in statements such as, if our T and A practice approaches excellence then . . . or, if diabetic acidosis treatment approaches excellence then . . . or, if treatment of unconsciousness approaches excellence then . . . or, if heart failure treatment approaches excellence then . . . Clearly there is a good deal of work to be done in merely establishing the criteria for excellence in medical practice.

It appears that a new pattern of medical staff organization is already being set up by the general disappearance of separate committees such as tissue committees, transfusion committees, and others covering areas of narrow concern. These are being embraced within the more inclusive approach offered by the medical audit. Furthermore, utilization evaluation will not call for an additional committee in the hospital which already has an active internal audit since the requirement for evaluation of utilization is satisfied by the medical audit. In contrast to merely curbing excessive use of facilities and services, the function of a utilization committee, the medical audit emphasizes also the impor-

tance of insuring that all patients receive all they need.

Medicine's drive has always been to insure for the next patient better care than given the last one. The rapid growth of biomedical science makes professional obsolescence a constant threat. It is for this reason that continuous education for the physician has become a compelling force. The evaluation process in the medical audit is itself a motivated form of continuous education for the physician. In addition to being springboards for staff's formal and informal education they undoubtedly must uncover many problems for investigation in clinical medicine.

L.H.N.

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## The Cell-Virus System

Since 1952 we have known that bacteriophage (virus) reproduces itself once it penetrates a bacterium, reproduces itself from its sole genetic material and gives rise to virions. This it does because inside the cell the nucleic acid molecule (the virus) finds enzymes, building blocks, a source of energy, ribosomes, for its own reproduction. It wasn't long before it was found that this was not a unique property of the bacteriophage, but a characteristic of all viruses. Thus it may be said that viruses are strict parasites which have created a remarkably new order to ensure their own perpetuation.

Lwoff explains that when the genetic material of a highly virulent bacteriophage penetrates a bacterium, the bacterial chromosome is destroyed and the bacterium becomes incapable of producing messengers and bacterial proteins. In the meanwhile, the DNA of the bacteriophage synthesizes its own messengers with the aid of ribonucleotides and enzymes of its host. Some of the proteins are enzymes necessary for the manufacture of specific constituents of the phage. Others are enzymes necessary for the replication of the bacteriophage DNA, and still others are structural proteins of the virions. The last one formed is endolysine which destroys and ruptures the bacterial wall thus ensuring the liberation of the virions. Everything takes place as if a system of repression and derepression were acting in sequence.

The bacterium infected by a virulent bacteriophage has become a virus factory which cannot be stopped except by its own disintegration. This is an extreme case because the relation between virus and bacterium do not always have this dramatic character. Some infected bacteria survive and perpetuate the ability to produce bacteriophages. These

are termed lysogenic bacteria in which the bacteria and the phage live in equilibrium. Thus once a virus enters a cell, the viral and cellular molecules confront each other and their fate is then decided in either one of two ways. Either the virus will multiply in the cell or the cell will enslave the virus. In short, it is either "total war or peaceful co-existence." How and why of peaceful co-existence was the big question Lwoff asked himself.

When he irradiated lysogenic bacteria with ultraviolet radiation the bacteria continued to grow for 45 minutes, then began to undergo lysis and in the process each of them liberated about 100 virions. What he had done was to induce phage reproduction in the bacteria which before were acting normally. The "prophage," the name given to the virus when it was in equilibrium with the bacterium, was converted into the bacteriophage which is a mortal disease. In short the silent-virus was forced by irradiation to express its full potentialities.

Previously we had thought that irradiation killed a cell because it destroyed an essential structure. Here irradiation was lethal because it actually triggered synthesis of virus which were lethal to the cell. Where then was the prophage located and what was its nature? Lwoff showed that it was attached to the bacterial chromosome at a well defined point, the so-called Receptor which is unique and specific for each type of virus.

The term "temperate" is given to a virus which infects a cell but lives with it in equilibrium. In such a case "the genetic material of the virus enters a cell, penetrates its cytoplasm, explores the bacterial chromosome, recognizes the receptor site and pairs with it." It becomes an integral part of the chromosome and behaves as if it were a bacterial gene. It is then reproduced by the enzyme which also reproduces the chromosome of the bacterium. If anything should be done to the cell to detach this new gene, then it may begin to reproduce with the help of local enzymes. What is the process by which lysogenic bacteria keep the infected virus enslaved?

The belief is that the virus attached to the chromosome produces a Repressor which is attached to the operator gene (Operon), the virus, and blocks the expression of the structural gene. This is necessary to prevent the virus from autonomous reproduction. A lysogenic bacterium can be made to produce virions, if it is derepressed as the irradiation did and as many chemical inducers are now able to do. Once the Operon, (repressed gene) is derepressed, it can express itself again leading to autonomous multiplication of the viral genetic material. Thus the repressor is really responsible for cellular immunity to viruses while

an inducing agent like irradiation acts by inactivating the repressor.

Lwoff explains that the fate of the bacterium-virus system depends on whether the repressor or the key enzyme responsible for autonomous multiplication is formed first, and this is determined in the first seven minutes after infection. But he points out that through the infection, the lysogenic bacterium has become a new organism, a cell-virus system whose fate will depend on certain aspects of its metabolism as well as on its environment.

People who occasionally exhibit herpetic infections harbor a cell-virus system. The infected individual usually presents no symptoms of disease. However, it will erupt under the influence of a great number of factors, although during the latent period there are no symptoms and it is not possible to detect the virus. During the latent period the viral cycle is blocked. A variety of "Inducers" all end up by derepressing the viral gene and allowing for its multiplication and manifest disease.

Just as there are inducers mentioned above, one would expect also to find the opposite namely inhibitors. Guanidine for example is known to inhibit the development of certain viruses and in particular poliovirus. Lwoff believes that it could act by inhibiting the synthesis of viral RNA through blocking transmethylase, the enzyme required for this synthesis.

Some viruses are oncogenic, the polyoma virus and leukemia virus for example. It is quite possible that they function as other viruses do and set up a cell virus-system. In our approach to treating cancer hitherto we have been occupied with finding substances which specifically kill the malignant cell and exclude the normal cell or else prevent the malignant cell from multiplying. There is, however, another obvious possibility if we reflect on what we know of the cell-virus system. Instead of attempting to repress the viral functions which also can repress vital functions in normal proliferating cells, we might attempt to intensify viral multiplication, so that the virus whose cycle is blocked thus permitting oncogenesis, instead, develops and kills the host cells, in short by seeking for derepressors.

We are still ignorant of the nature of the factors which govern the relation of oncogenic virus and cell. But only a few years ago we were also ignorant of the effector sites on the gene to which virus attaches. We were also ignorant of the repressors which prevent multiplication as well as of derepressors which free the virus to grow and destroy the cell. Such research must be developed and extended. Perhaps this will be the way towards the destruction of the oncogenic virus and its cell host.



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It can be seen that terms are appearing which were not thought of when many of us studied our basic sciences. Operon, effector sites, repressors, de-repressors, inducers, etc. We may take pleasure in understanding some of these newer terms solely for the pleasure of knowledge. But one can see a promise of eventual fruit for the practice of rational medicine as well, and how the great minds like Lwoff's function in pushing the frontier of knowledge forward. Ribosome, operon, messenger RNA, transfer RNA weren't used by medical students 15 years ago, but such terms we must understand for a grasp of modern microbiology, which is already revolutionizing biochemical sciences, genetics and oncogenesis.

L.H.N.

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## A Key To Antibody Formation

Certain cells produce antibodies in response to a foreign antigen which enters the blood stream. It is through the body's ability to make an almost unlimited variety of these molecules that permits it to ward off many diseases. The main antibody produced in the circulatory system in response to the challenge of foreign antibodies is gammaglobulin (GG) of which there may be many thousands of varieties but they all have a common molecular weight of 150,000 and they are all remarkably similar in their structural properties.

Each GG molecule consists of a long chain of aminoacids. There are only twenty varieties of aminoacids but their sequence can vary and this permits infinite variability in the structure. It is this fact that makes one kind of antibody differ from others. It is this fact which makes it difficult to understand the method by which they are formed.

According to Dreyer and Bennett the genetic procedure which governs antibody formation "is radically different from anything normally found in modern molecular genetics" and therefore they have been led to propose a new theory about genetic behavior among antibodies, which if it turns out to be true will take biochemistry a step closer to understanding how antibodies are formed with such diversity.

Ordinarily G.G. consists of four subunit polypeptide chains (see figure on cover page). Two of these chains are identical molecules with molecular weight of about 25000. These Dreyer calls L chains. Two other H chains are twice the weight of L chains. The sequence of aminoacids in these

chains is organized in such a way that the molecules fold themselves into configurations that allow them to interact with each other to form half molecules. These in turn combine to form complete G.G. structures. The sites that contain the antibody specificity are at both ends of the molecule.

Chemical studies aimed at determining the molecular basis of the different G.G. have thus far been handicapped because of the molecular heterogeneity of G.G. Now biochemists have been able to delve more deeply into the structure of antibody molecules. In multiple myeloma the plasma cells secrete a homogeneous protein, the Bence-Jones protein, which is in fact the L chain of G.G. Thus by studying this protein Dreyer and Bennett were able to carry out chemical studies on homogeneous L chains which it was not possible to do before.

They find that about half of the amino acid sequence in these chains, taken from a strain of inbred mice with multiple myeloma is always identical with corresponding portions of all other Bence-Jones protein chains, while the remaining part contains a different set of peptides which distinguishes it from any other protein sample. Stated another way the G.G. molecules consist of uniform portions the L chain common to all antibodies of this type together with active areas that vary between molecules.

It is possible to think of a model, the key and the lock. The portions of the antibody molecule that differ from antibody to antibody, form a specific "slot" into which only one kind of antigen can fit. This slot is like the tumbler in a lock which differs in each lock and reacts only when the proper "key" or foreign antigen comes into contact with it. It is the variation in these lock "tumblers" in the antibody that accounts for the vast array of antibodies possible.

The simplest genetic explanation of how such a wide variety of antibodies can be formed in the body would be that many thousands of different genes each produce a different antibody molecule. Dreyer and Bennett found that this actually is not the case. They believe instead that the variable end of the L chain behaves as if it were made by the genetic code contained in any one of more than 1000 genes. The other end, the part that is common to all L chains, seems to be the product of a single gene. This view would imply that a special kind of genetic rearrangement must occur during the development of separate antibody producing cells.

In contrast to many of the older theories, it is Dreyer and Bennett's view that the ability of a body to produce a given kind of antibody molecule is inherited. This implies that our ability to de-

fend ourselves against a particular disease is the result of molecular evolution which has taken place over many millions of years.

If this idea on antibody formation proves correct, it may provide some of the knowledge needed to manufacture antibodies in laboratory, a development that could revolutionize medicine. Methods are already available for synthesizing small molecules of short chain aminoacids as for example angiotensin. It cannot be too long before these methods will be extended to permit syntheses of much larger chains of aminoacids such as those needed in the manufacture of antibodies. One can

speculate that perhaps a globulin will be found that can neutralize many antigens rather than just one.

If and when man-made machines can manufacture antibody molecules directed against specific disease organisms, man will be able to protect himself against new diseases, long before his body could develop its own antibody.

L.H.N.

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## THE PRESIDENT'S MEDICARE CONFERENCE

*Orvan W. Hess, CSMS president, was one of the "medical and hospital leaders" who was invited to attend President Johnson's White House Conference on Medicare, June 15, 1966. The following are some of Dr. Hess' impressions of the meeting.*

As the day of activation of Medicare approaches, some important implications of the law fall into focus more clearly. It is essential that new relationships that will be created between physicians, hospitals, and the government be recognized if misunderstandings and disappointments are to be avoided.

President Johnson, at a recent White House Conference on Implementation of P.L. 89-97, referred to the launching of Medicare as an historic event. Indicating sincere pleasure with the promise of potential benefits for those aged 65 or older, he nevertheless warned of the consequence of abuse. This anxiety is understandable. Misuse of privileges, largely dependent on individual conscience, has been experienced by voluntary insurance agencies. Some, on the brink of bankruptcy, found it necessary to increase premiums. In the case of financing via the government, under provisions of the Medicare law, preservation of fiscal solvency under similar conditions could necessitate further increases in Social Security contributions. Since this problem is related to financing, it is mainly of concern to the actuaries. It is not the responsibility of the physician, other than as a private citizen and as a contributor to Social Security. Monitoring of certification for admission and duration of confinement to health care facilities will be carried out by utilization committees comprised of physicians.

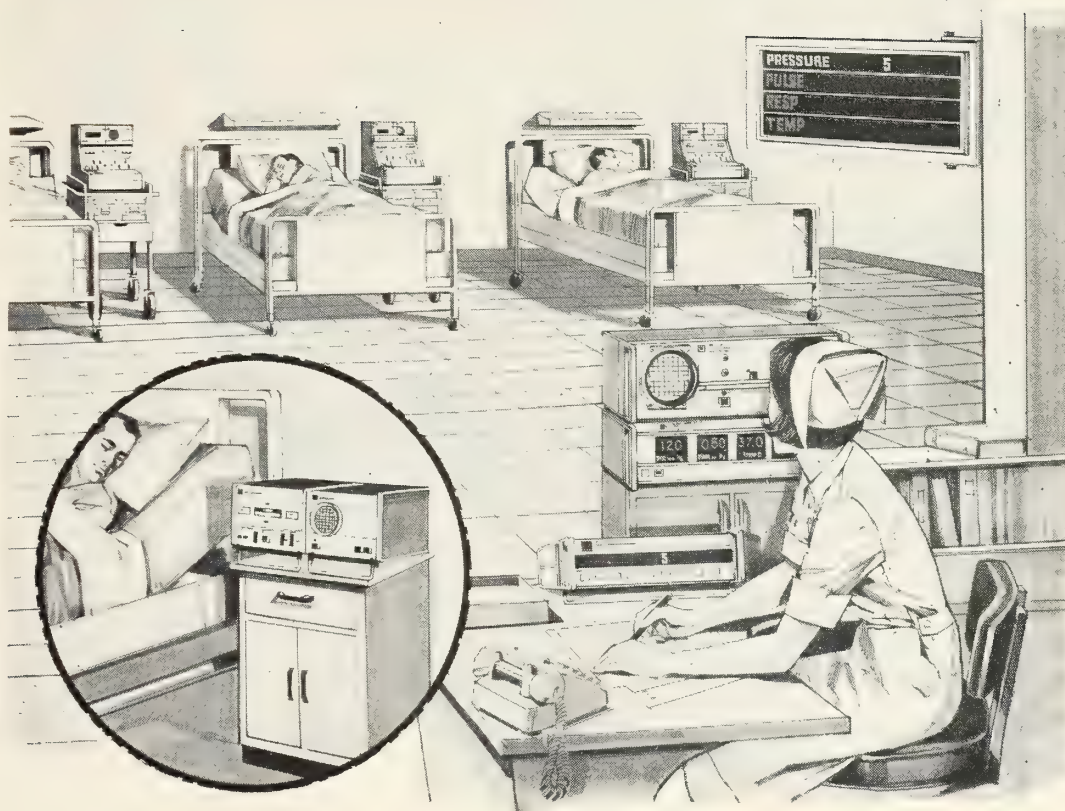
However, judgment of the needs for proper care, kinds of medications, etc., regardless of cost, will still rest with the doctor.

Maintenance of the optimum relationship between physicians and hospitals, and other health care facilities, will require the greatest mutual effort. Since the hospital bed occupancy by patients 65 or older is now 25 per cent and will increase, the burden on hospital administrators will be even more acute. Some hospitals have not yet met their responsibilities to the community physician in providing sufficient beds or adequate personnel (nurses, anesthetists, para-medical assistants). For this reason the public has suffered inconveniences and possible physical harm from delay in admission. At the same time there has been inefficient use of available time and talents of existing physician-manpower. With the government now assuming the costs involved, there seems little excuse for further procrastination.

To successfully implement the Medicare law a high level of cooperation will be required. It is apparent that well-defined areas of responsibility exist for the Federal government, physicians, hospital and extended care facility administrators, and the public.

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# Nephroblastoma And Neuroblastoma, A Current Concept In Recognition and Treatment

Lawrence K. Pickett, M.D.

■ In the consideration of all the malignancies of childhood, if one excludes leukemia and other blood dyscrasias as well as central nervous system tumors, the most common malignancies encountered are: (1) the nephroblastoma, also known as an embryoma, mixed tumor, or Wilms tumor, and (2) the neuroblastoma, the general term which describes tumors of neural crest origin. The most primitive or undifferentiated form of this group is the sympathicoblastoma or sympathicogonioma, and a more mature and rarely malignant form known as the ganglioneuroma. Although the nephroblastoma arises consistently within the renal parenchyma, the tumors of neural crest origin may occur anywhere along the sympathetic chain from the neck to the pelvis, in the adrenal, and occasionally, most prominently in the liver. Although this latter is assumed to be a metastatic site, the primary may be difficult to find. Since the embryoma and the abdominal forms of neuroblastoma occur principally as asymptomatic abdominal masses, they both must be considered in differential diagnosis, in addition to a common abdominal mass, that of hydronephrosis. Since the histology and clinical behavior of the tumors varies considerably, they will be discussed separately.

## Wilms Tumor

The nephroblastoma or Wilms tumor is characteristically described from a pathological standpoint as a mixed tumor with tremendous variation in the cell type. All cellular patterns, including those of carcinoma, sarcoma, myxoma, rhabdomyoma, and cells of neural origin are found in varying degrees, in addition to incompletely formed nephrons, appearing principally as abortive tubular formation.

It never has been possible to make an absolute correlation between the histopathology of these tumors and their clinical behavior, although those that are primarily sarcomatous or have a large component of muscular elements are generally less radio-sensitive and, also, less sensitive to the chemotherapeutic agents. These tumors may appear multicentric in origin, and from five to ten per cent of the various series reported indicated bilaterality; an important consideration in the therapeutic approach. Since these are embryonal tumors, their presence since birth is undisputed. Remarkably

abrupt increases in size, however, have been noted, presumably due to some poorly understood disruption of the tumor-host relationship.

## CLINICAL BEHAVIOR

Most of these tumors become evident in the first five years of life, some being detected at birth, and an occasional one as late as seven or eight years of age. Most series indicate a predominance of the females. Sex is not a determining factor in the survival rates, whereas, the age of the patient at the time of the appearance of the tumor has a remarkable influence on the outcome; those that occur in the first six months or year of life have a relatively favorable outlook with survival rates between 85 and 90 per cent recorded in many series.<sup>5</sup> The older the child at the time of surgery, the less likely survival becomes, probably as a function of a prolonged period for possible metastases.

The recognition of these tumors is generally occasioned by the presence of an asymptomatic abdominal mass in the majority of cases. This is generally not associated with the usual signs of malignancy, i.e., fatigue, pallor, anemia, loss of weight, anorexia, or pain. Any of these symptoms may occur; however, they are relatively uncommon. Hematuria may be a presenting symptom or when found in a course of the evaluation of the patient, it has a bad prognostic significance.

Hypertension is, also, present in a large majority of the children so afflicted but is rarely a symptomatic occurrence.

## DIFFERENTIAL DIAGNOSIS

Since the tumor generally appears as an asymptomatic abdominal mass, it must be differentiated from hydronephrosis, other intra-abdominal masses such as duplication of the bowel, mesenteric cyst, omental cyst, or other retroperitoneal masses such as teratoma or sarcoma. The X-ray evaluation is the ultimate definitive diagnostic tool. A plain film of the abdomen discloses displacement of the abdominal contents medially and from behind; it is rare to have calcification in a Wilms tumor and, also, rare to have it extend across the mid line. In-

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FIGURE 1A

Intravenous pyelogram showing calyceal distortion of left kidney. Stomach is displaced medially. Films are diagnostic for Wilms tumor.

dentation upon the stomach, posteriorly displacing it anteriorly and medially, is common in left-sided masses. Confluence with the liver shadow on the right makes a differential diagnosis between a renal and hepatic mass of primary importance. Following the plain film of the abdomen, an excretory urogram — intravenous pyelogram — is the single most useful X-ray examination; since the tumor has an intra-renal origin, the calyceal system in the Wilms may be totally obliterated or, more commonly, distorted and sometimes displaced. This is to differentiate it from the usual appearance of an adrenal tumor such as neuroblastoma which causes total displacement of the renal shadow without internal distortion of the calyceal pattern. The intravenous pyelogram serves to differentiate embryoma from hydronephrosis on the basis of an ureteropelvic obstruction or a double-collecting system with a hydronephrotic lower pole. A chest film is an essential, since the Wilms tumor characteristically metastasizes first to the lungs. Metastatic surveys of the long bones generally done are usually helpful in yielding only negative information. It is rarely necessary to confirm the findings of an intravenous

pyelogram by a retrograde study, although this may occasionally be indicated in the absence of any function on the side of the mass. Although the approach to a massive hydronephrosis of this sort is not unlike that of a Wilms tumor, the prognostic significance of the approach is important, as the surgeon might be inclined to use a flank incision in the case of hydronephrosis; whereas, the trans-abdominal approach with immediate attention to the vascular pedicle of the tumor is indicated in the case of the malignancy. In the vast majority of the cases, no further diagnostic efforts should be made. Surgical and chemotherapeutic approach to the tumor can be undertaken immediately. Needle biopsy is to be condemned, since this may violate the tumor and make local spread a likelihood. When the capsule is intact, this is an extremely unusual source of spread of the disease.

#### TREATMENT

Prior to the introduction of Actinomycin D, and more recently, Vincristine, in treatment, surgery plus postoperative radiation to the tumor bed was



FIGURE 1B

Characteristic lung metastasis in a nine-year-old girl with left Wilms tumor. (Courtesy of Dr. William Gryboski, New Britain, Connecticut.)



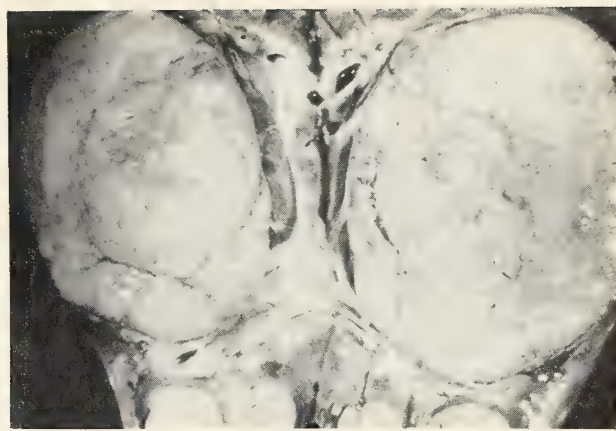
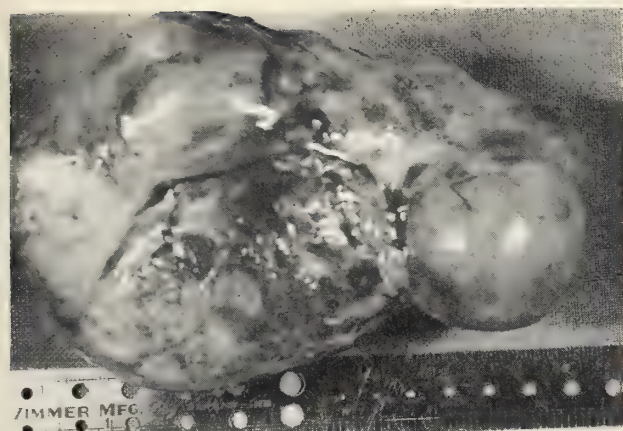


FIGURE IIA AND FIGURE IIB

Photograph of Wilms tumor showing multicentric origin with separate nodules of tumor.

the most successful approach to the problem. Sporadically, throughout the history of the disease, preoperative radiation has been suggested to reduce the size of the tumor, but this has fallen into disuse because of the occasional misdiagnosis, and theoretical, if not actual, chance of metastasis during the radiation therapy, and the most powerful argument, that of therapeutic success, since the most successful series in the literature prior to chemotherapy as presented by the Boston Children's Hospital<sup>5</sup> using X-ray following surgery and not before. Since Farber's<sup>2</sup> original report on the effectiveness of Actinomycin D in metastatic Wilms tumor, and more recent reports on the effectiveness of Vincristine, these drugs have been added to surgery and radiation — an overall improvement in the long-term prognosis. Actinomycin D and X-ray seem to have a somewhat synergistic effect, and when used in combination, both dosages should be decreased.

In view of the effectiveness of Actinomycin D in treating metastatic Wilms tumor, it has been felt, recently, that the use of this drug in the preoperative state, even without a tissue diagnosis, is indicated. Reports from Australia,<sup>9</sup> Houston,<sup>3</sup> and elsewhere indicate that Actinomycin has been given in a dosage of 75 micrograms per kilogram divided in five doses. The first three doses were given daily prior to surgery, then surgery was performed, and with confirmation of the diagnosis, the remaining two days of therapy were given followed by irradiation to the tumor bed and to pulmonary metastases, if such be present. Radiation therapists have been accustomed to giving between 3,000 and 3,500 roentgens to the tumor bed following surgery. When given in combination with Actinomycin, most agree that radiation dosages must be decreased to about 60 to 75 per cent of the total dosage. Since both Actinomycin and radiation are serious bone marrow depressants, close evaluation

of the marrow depression by daily cell counts in the peripheral blood is the best indication of danger. Farber has felt that the platelet count is the most sensitive index. Others feel that white cell depression and red cell depression are equally valid. Repeated bone marrow aspiration and absolute counts of cellular elements are helpful, but the peripheral hematologic picture is generally adequate for close following and evaluation. Actinomycin D is associated with a considerable number of side effects which may be anticipated with stomal ulcers, loss of hair, anorexia, nausea, vomiting, and some weight loss. Although the drug is immediately effective, maximum effect continues for approximately 21 days, so that radiation during this period must be done somewhat carefully.

#### RESULTS

The results, in the larger series,<sup>8</sup> have shown a considerable increase in survival secondary to the use of Actinomycin in the overall group, and those treated without selection, including those with multiple metastasis at the time of the removal of the original tumor, between 60 and 75 per cent of the patients had had survivals for a period long enough to be considered cures. In the younger age group, without metastasis being present at the time of presentation, expected survival is considerably higher. Definitive figures are not yet available, however, on the overall effect of Actinomycin, since the drug has been used repeatedly in many cases with suppression of the tumor but sufficient time has not elapsed for it to be evaluated as a curative agent.

Recently, reports have shown that Vincristine, a derivative of the periwinkle plant, is, also, effective in treating metastatic Wilms tumor.<sup>12</sup> No series is large enough for evaluation as yet, but the alternative use of Vincristine and Actinomycin is advocated in cases where recurrence is evident.

Each of these drugs seems to have a decreasing potency with repeated usage and, thus, the alternation may lead to more prolonged palliation and, occasionally, cure.

In the case of metastatic disease in the lung where a long enough period of observation has allowed the assumption that metastasis is solitary and detailed studies of the chest including laminography indicate no other lesions present, surgical extirpation of the segment of the lung involved by the lesion is indicated. Since it is far more rare for metastatic lesion to be single than to be multiple, this would seem to be the unusual case in which surgical therapy is warranted. With the addition of Actinomycin, radiation therapy to a localized lesion of the chest or to numerous lesions has been possible without the serious after effects of radiation fibrosis, so common in previous attempts to radiate pulmonary metastatic lesions.

An additional word may be said for the surgery of bilateral Wilms tumor; more commonly one side is considerably larger than the other, and this has been removed surgically with dependence on the Actinomycin and minimal X-ray therapy for control of the contralateral lesion. Radiation therapy must be used with great care in the single remaining kidney, as radiation nephritis is as fatal as the malignancy. Direct profusion of the renal artery has been suggested and attempted, but no well-founded program can be advised at the present time because of a paucity of experience.

The addition of Actinomycin to radiation in no way circumvents the need for early and careful surgical excision with the earliest possible interruption of the venous drainage of the tumor during excision. Great care to avoid violation of the capsule is paramount in importance from the surgical standpoint.

In summary, using a combination of surgery, postoperative radiation and chemotherapy including Actinomycin D and Vincristine, the outlook for children with Wilms tumors has been improved. Too much attention can not be paid to earlier recognition and prompt surgical therapy to intra-abdominal masses of this sort.

### Neuroblastoma

#### **PATHOLOGY**

The neuroblastoma is characteristically made up of small, heavily-pigmented cells with very poor differentiation, occasionally forming pseudorosettes. The appearance varies from the most undifferentiated type of tumor, those of the sympathicoblastoma or sympathicogonioma where undifferentiation and difficulty in diagnosis is the hallmark to the far more differentiated tumor made up almost completely of cells resembling the mature ganglion cells of the sympathetic nervous system.

Three types of tumors are recognized, the pure sympathicoblastoma and neuroblastomas, on the one hand, and a mixture of neuroblastoma and ganglioneuroma, referred to in the literature as ganglioneuroblastoma, and finally, the more mature and generally benign form of ganglioneuroma. A concept of maturation of the tumor from the most undifferentiated form to the more benign form has been entertained and accepted in the past.<sup>1,10</sup> No true control study has shown that this occurs in any individual case. The possibility of various forms of this tumor arising from different primitive cells from the neural crest probably has more validity.

These tumors do commonly exhibit hemorrhage and necrosis and, indeed, many documented cases in the literature prove that they may destroy themselves totally and resolve spontaneously, although not with regularity enough to allow any form of watchful waiting in their therapy at the present state of knowledge.

#### **CLINICAL RECOGNITION**

Whereas, most of these tumors manifest themselves by the presence of an abdominal mass, they are more commonly associated with anemia, low-grade fever, abdominal pain as well as hypertension. On initial discovery, the tumors are generally far more irregular than the nephroblastoma, somewhat more fixed, and tend to cross the mid line as opposed to previously described masses. Again, in this group of tumors, there is a predominance of females over males, and most of the children are in the early part of the first decade of life when the tumor is discovered. Massive infiltration of the liver is occasionally seen in newborns, but the tumors of the adrenal medulla and other sites in the sympathetic nervous system generally do not appear until after the first year of age. There is a prognostic significance to the position of the occurrence of the tumor. Those in the chest, neck, and at the bifurcation of the aorta seem to have a better prognostic outlook than those appearing in the adrenal medulla.<sup>6</sup> Those occurring primarily as replacing the liver seem, also, to have a more favorable outlook.<sup>13</sup> Metastasis in the case of neuroblastoma is primarily to bone, and in the absence of X-ray evidence of destruction, bone marrow aspiration may show abnormal cells. Pulmonary and other organ metastases are late in the history of the tumor. Anemia, weight loss, low-grade fever, and increased abdominal girth may be the presenting complaints in addition to anorexia and occasional nausea, vomiting, and abdominal pain.

#### **DIFFERENTIAL DIAGNOSIS**

As mentioned above, abdominal masses should be differentiated from hydronephrosis, intra-abdomin-



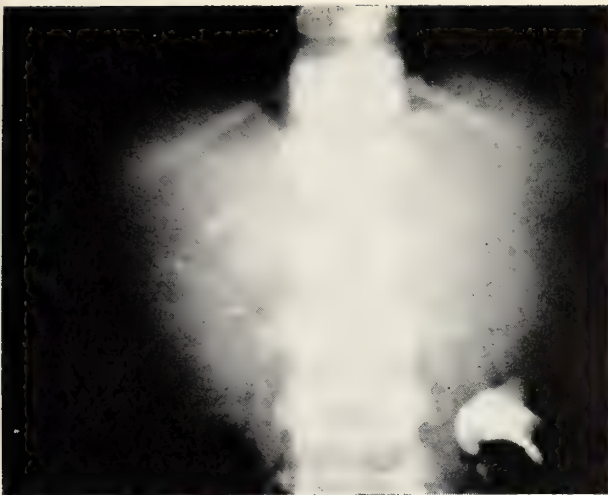


FIGURE IIIA

Intravenous pyelogram showing downward displacement of intact calyceal pattern on the left, characteristic of neuroblastoma of adrenal origin.

al cysts, and genital ridge tumors. Again, the intravenous pyelogram or excretory urogram is the most valuable examination, giving a more uniform displacement of the entire renal shadow in the case of the adrenal site for the neuroblastoma. Calcification within the mass is somewhat diagnostic. Cervical or posterior mediastinal masses and those arising in the hypogastrium, palpable by rectum, have no peculiar appearance by X-ray but must be considered in the differential diagnosis of neuroblastoma by their position.

A small number of children may present with intractable diarrhea as the only symptom. A search for an origin of the tumor should be undertaken. Recently, in addition to the above diagnostic signs during the course of the study in one of the children with an intractable diarrhea, it was found that the tumors of neural crest origin are functional tumors and produce an excess of the catecholamines.<sup>4</sup> Work done by Gardner, Voorhess,<sup>11</sup> et al. has shown that all of these tissue types of tumors may produce excessive catecholamines, either the precursors including dopamine and norepinephrine or the metabolites, metanephrine, normetanephrine, homovanillic acid (HVA), and vanilmandelic acid (VMA). Since most of the tumors will produce an increase in the metabolites of the catecholamines, screening in the presence of an abdominal mass, chest mass, or diarrhea by the studying of the VMA might be undertaken. No tumor, however, highly suggestive of this group of neural crest tumors should be ruled out without the total study of all of the elements of catecholamine metabolism because of the small group that produces only the precursors and a much smaller group that does not produce catecholamines detectable by the

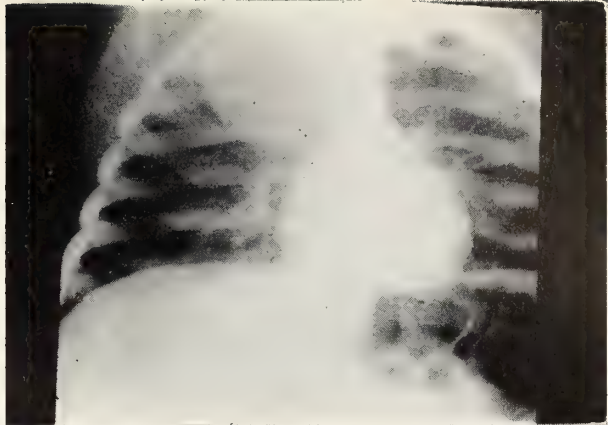


FIGURE IIIB

Chest film showing posterior mediastinal mass proven to be ganglioneuroblastoma. This patient had diarrhea as a presenting complaint. Catecholamines were elevated markedly and returned to normal following resection. The patient is surviving six years later and presumed cured.

present methods. The study of the catecholamine pattern in the tumor is important, not only from the diagnostic standpoint but also from the therapeutic, since this is a valuable measurement in relation to the clinical effectiveness of the treatment. Preoperative levels as compared with serial postoperative determinations are essential in the proper therapy for these tumors.

#### CLINICAL TREATMENT

Following the X-ray evaluation, and here again, retrograde pyelography is seldom necessary for achieving the maximum information, marrow aspiration is done to be sure that there are not distant metastases not evident by X-ray, and surgery is undertaken. Only rarely is the mass excisable, since this is an insidious tumor which seems to invade adjacent structures, cross the mid line, and involve vital vascular structures more commonly than does Wilms. Often, a simple biopsy followed by radiation, since these tumors are uniformly radiosensitive, is the preferred treatment rather than life-threatening surgery which, due to the nature of the growth of the tumor, rarely accomplishes complete removal. Koop et. al.<sup>7</sup> have suggested morcellation and removal of as much of the tumor as possible as the sole form of treatment not followed by radiation and chemotherapy. This series is not great enough or documented with results that warrant adopting this form of treatment. Radiation should include the entire area as outlined by silver clips at the time of surgery to encompass all of the tumor. In addition to radiation, cytoscyphosphamide (Cytosan®) has been found useful in suppressing the growth of the tumor. Since this is not synergistic with X-ray, but is a severe marrow depressant, it must be used with

some caution but not with the same diminution of X-ray dosage as with Actinomycin D.

Many chemotherapeutic agents have been effective in the hands of various investigators; nitrogen mustard, Velban® or vincoleucoblastinesulfate, and Vincristine have all had sporadic favorable reports. Differing from the nephroblastoma and the increase in survival secondary to the use of Actinomycin D, the chemotherapeutic agents have not proved as favorable in the tumors of neural crest origin. They have, however, been useful in palliation and, have played a major role in tumor control awaiting a secondary surgical approach.

After the initial biopsy excision, radiation therapy and cyclophosphamide, serial determinations of the catecholamines can give one evidence of the effectiveness of treatment. Should these not revert to a normal level (and normal should be determined by the age of the patient and not related to adult levels), perhaps, a secondary surgical approach may be possible with the favorable effect of X-ray and chemotherapy as well as, possibly, the maturation of the tumor.<sup>11</sup> Several cases in the literature have been reported with "second look surgery" with the excision of the remaining tumor, not possible at the first exploration. When bony metastases have become evident by X-ray, there are practically no reported survivors. X-ray therapy can be used to the metastatic sites as a palliative measure.

The overall survival rates of this group of patients ranges between 20 and 35 per cent, depending upon the age at the time of discovery. Again, final evaluation of the chemotherapeutic agents has not yet been possible. As with the Wilms tumor, it has been suggested that alternation of Vincristine and Cytoxan seems to potentiate the action of both and, perhaps, is useful in the palliation of the tumor.

In summary, tumors of neural crest origin may appear as abdominal masses or asymptomatic masses along the chain of the sympathetic nervous system.

Most of them produce catecholamines and can be detected by the evaluation of the catecholamine

levels in the urines. Therapy is by surgery, radiation therapy, and chemotherapy with a guarded prognosis in the light of present knowledge. Extensive and life-endangering surgery is not indicated in neuroblastoma. Hopefully, control and palliation may allow maturation of the tumors from the malignant to the benign form, although this remains unproven.

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# Viruses And Human Neoplasia

Melvin Horwitz, M.D.

■ As far back as the 17th Century the infectious theory of etiology of cancer was advanced. It is interesting to note that a Dr. B. Peyrilhe, Professor at the Royal College of Surgeons in Paris, received a prize from the Academy of Sciences in Lyons for his paper on the infectious origin of cancer.<sup>1</sup> He attempted to transmit human cancer to a dog by taking a few drops of fluid from a breast cancer and injecting it under the skin of the animal. Swelling and discoloration appeared and progressed during the next five days. However, the suffering animal was drowned by the physician's servant, and while the animal had obviously developed only an abscess, it indicates nevertheless the early interest in the infectious nature of this disease. We are still interested in this approach. The National Cancer Institute currently spends over 28 million dollars for the support of virus-cancer research in the United States and in the past year has undertaken a special virus leukemia program, whose overall design is similar to that of the industrial systems research programs.

The underlying assumption in all of this work is that the development of cancer, leukemia, or other malignant tumors is the result of an activation of at least one virus which then acts as an oncogenic agent (either directly or indirectly), producing at least one kind of malignancy, and that the virus will persist in the diseased individual in one form or another.<sup>2</sup> The virus may have been activated merely by accident and may well have been carried by the host since birth, indeed, may have been transmitted to him via the germ cell from his parents.

## The Evidence

The viral etiology of many types of malignancies is fairly well established in many different kinds of lower species of animals and in other species such as fish, possibly in frogs, and in many plants. In some of these animals, especially the chicken, mouse and hamster, Koch's postulates have been fulfilled: 1. The infecting organism must be present in all cases; 2. Innoculation in pure culture must produce the same disease; 3. One must be

able to obtain and propagate the original organism in pure culture. In the leukemias, virus has been demonstrated by bio-assay, electron microscopy, and immuno-assay prior to the onset of the clinical disease, during the clinical disease, and in tissue culture of malignant cells of the leukemic line. Production of the disease consistently follows inoculation with cell free virus preparations. The morphology of the various carcinomas, sarcomas, leukemias, etc., are very similar in man and the lower animals, and the clinical courses are also parallel. In many medical schools the pathologist of a nearby animal hospital will several times a year lecture to the medical school class and reproduce most of the human diseases, both malignant and nonmalignant, in his animal population. Epidemiologically, the similarity of malignant disease in man and animal is very striking, as is the response to effective treatment, i.e., most of the effective anti-leukemic drugs used in human leukemia are also effective in murine leukemia.

Before detailing the above I should like to point out some of the problems in working out the viral etiology of tumors in man. Man is a very heterogeneous animal with a relatively long life span, who usually reproduces slowly and infrequently (though this may be disputed by some) and in whom family records and histories are not well kept. Looking back at Koch's postulates it is obvious that the oncogenic activity of human viruses will have to be determined by a suitable laboratory bio-assay or immuno-assay methods rather than species inoculation. We know from animal work that one can increase or decrease the susceptibility of the host by varying the environment or by the application of chemicals, drugs, radiation, etc. We know also from animal work that the virulence of the virus, as related to tumor induction, is also a variable factor. Infection in the animal with the virus can occur without the production of a tumor. Tumor viruses can be replicated in very large amounts by many cells within the body which do not themselves undergo malignant transformation. These cells which are parasitized by these viruses but seem to show no ill effects, are frequently those that produce large quantities of proteins, such as

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*Supported in part by a grant from the Gertrude H. Rogers Fund.*

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the acinar cells of the pancreas,<sup>3</sup> megakaryocytes<sup>4</sup> of the spleen and marrow and epithelial cells of the mammary glands.<sup>5</sup> The recent isolation of the mycoplasmas (PPLO)<sup>6,7,8,9</sup> and virus particles in leukemic cells, or cells reproduced in cell culture from leukemic patients, raises many interesting questions. The virulence of the tumor viruses may also be effected by its replication in cell culture. Work of The Charles Pfizer Company has shown that using cell lines from a mixed mouth, thymus and spleen tissue culture which supported several murine leukemia viruses, but only producing small amounts of virus, suddenly changed and began producing large quantities of virus.<sup>10</sup> Also of interest was the fact that a subline of one of these (JLSV5) continued to produce large quantities of virus with little or no leukemogenic infectivity. Mice inoculated with this virus did not develop leukemia and appeared to be completely resistant to challenge with another active virus (Rauscher). While this is preliminary data, only recently reported, it may be one of the first examples where attenuation of a tumor virus is not related to the decrease in number of virus particles. On the other hand, it is well known that increasing the number of virus particles in the inoculum increases its virulence in some attempts at cross-species infection. In addition, some viruses are made more virulent by serial blind passage from one generation to another within the same species. Occasionally cross-species passage of a virus or tumor cell line will increase the yield of virus or increase its virulence, or both. (It might be noted here that this possible increase in virulence of the virus may well be one of the major hazards in the development of a human tumor-viral vaccine.)

Other studies which may both explain some of the variations seen in tumor production in animals and man, and yet make evaluation of results, particularly in man, difficult, are as follows:

Gross has reported that thymectomy in C3H mice injected with his leukemia agent, may result in granulocytic, rather than lymphocytic leukemia, and some of these only develop after a long latent period. It also has been shown that avian myeloblastosis virus is pleiotropic in young chickens, the same agent causing such varied conditions as leukemia, a kidney tumor similar to Wilm's tumor and osteopetrosis, a condition resembling Caffey's disease.<sup>11</sup> It also has been shown that the Rous Sarcoma Virus is a defective virus.<sup>12</sup> It does not become oncogenic until a protein coat is produced with the aid of associated viruses, each of which may produce a different coat and thereby a different type of tumor. (Is this the explanation of the fact noted that in some cancer families, relatives will develop different types of tumors and leukemia

and how is this related to varied host factors, both environmental and genetics?)

### **Viral Particles In Human Tumors**

Many investigators have demonstrated particles in humans that are similar to mouse Leukemia viruses in electron micro-photographs of thin sections of lymph nodes, marrow, peripheral blood and pellets from plasma concentration studies.<sup>1,13-18</sup> These have mainly been Type "C" virus particles which measure approximately 100 mu. These particles have been present more often in human leukemics than in non-diseased humans or in other patients with no leukemic blood problems.

Fink and Malngran have developed an immunofluorescent technique which can detect viral leukemia antigen in leukemia cells in mice.<sup>19,20</sup> Antisera conjugated with Fluorescein Isothiocyanate were prepared against mouse leukemia viruses and this antisera was used to detect and quantitate the amount of fluorescent antigen in the cells of mice infected with murine leukemia viruses. Using similar techniques, antisera have been prepared against purified concentrates of human leukemic plasmas shown by electron microscopy to contain type C viral particles. These techniques detected fluorescent antigen within the cells of the peripheral blood and tissues of approximately 50 per cent of human leukemics and in established tissue cultures from tumor biopsies of Burkett lymphoma patients.<sup>21</sup> They were not found within cells of normal persons or of persons with other nonmalignant diseases. In 50 cases of human leukemia studied by Rauscher, Fink and Malngran, immunofluorescence was seen in blood smears of all but one of those where type "C" virus particles had been seen in the plasma on electron microscopy. Fluorescent antigen-antibody cross reactions and neutralizing activity has been noted in some human leukemic sera against avian and/or murine leukemia viruses (Rauscher).

### **Tissue Culture And Bio-Assay Studies**

Many attempts have been made to take cell free filtrates from leukemia and other malignant disease patients and concentrate and inject these into animals. In several different studies some of the respiratory viruses (SV) have produced tumors in hamsters and some other animals. There has been no direct evidence of the production of a human tumor by this material. In some early studies, tumors were found in some animals, and eventually viruses were found which caused these tumors. These proved to be an original animal virus that had been carried by serial passage from animal to animal and eventually became more virulent. (Grace)



## Human Tissue Culture

A more recent significant step has been made in the direction of human tumor tissue culture: In several different laboratories human neoplastic cells have been established in tissue culture.<sup>25,26</sup> Most of these have been leukemia or lymphoma cells, but sarcoma and carcinoma have also grown. There are many similarities between these cells and Murine leukemic cells morphologically and immunologically. In more than half of these human cell lines, virus particles have been found on electron microscopy, and serologic testing has established that they are unrelated to any of the known groups of human or animal viruses. It is interesting to note that attempts have been made for many years to grow human tumor cells in tissue culture. It is perhaps only by chance that researchers have been successful. Initial tissue culture studies usually grew cells on the glass walls of the containers, and if none appeared it was felt that none were growing. Recently, by trial and error attempts at changing the culture fluid, the discovery was made that some of these cells were in the fluid rather than on the glass. This ability to culture cells is a great step forward in delineating the etiology and microbiology of human tumors. One must certainly begin to consider that these particles which are almost certainly viruses are related to human malignancy. An additional supporting factor is that several of these particles seem to share a common immunofluorescent antigen (Fink). They appear somewhat similar in morphology and size, and all appear to mature within the cytoplasm of the cells. To dampen one's enthusiasm along this line is the fact that the virus particles detected in the human leukemia tissue cultures are perhaps morphologically more similar to the herpes viruses whereas those particles found in the Murine and Avian leukemia tissue culture and in the centrifugal residual pellets of human leukemic plasmas show type "C" morphology. However, while varying virus particles may differ in appearance and chemical composition, etc., they still may produce the same type of diseases depending again upon external environmental factors and host factors such as genetic makeup, age, species, etc. Both polyoma and Rous sarcoma viruses, given in large enough quantities can induce fibrosarcoma type tumors of similar morphology in hamsters. It is of course possible that the particles seen in the tissue culture and indeed in the plasma and marrow studies of human leukemia patients are merely passenger viruses with no causal relationship to human tumor. In some of the cell lines there is a common fluorescent antigen, not found in tissue cultures infected with PPLO, Herpes or Myxovirus and the etiology of this antigen and the virus particles seen in human tissue culture tumor cells, is still to be

determined.<sup>21</sup> In the recent literature mycoplasma (PPLO particles)<sup>7,9</sup> have been described in human tumor patients and in human leukemia cell cultures. The relationship of these particles to human tumors is still unknown.

One final thought before leaving the bio-assay studies of viruses in human tumors: One must always return to basic principles such as Koch's postulates and again the difficulties in working with a particle as small as the virus is evident. Differentiating an injected human tumor virus from an endemic animal neoplastic virus is very difficult. Certainly, morphology may not be the answer, and we will have to resort to immuno-assay techniques.

## Epidemiological Evidence

Clinical observation over many years has made it difficult for workers in the human tumor, animal tumor and oncogenic virus fields to accept a "contagious" origin and spread of malignant disease. However, it is well known that there is spread of animal tumor viruses from one host to another even though spread and infection with the oncogenic virus need not be followed by the development of a malignancy. For example, the polyoma virus is usually harmless for most of its natural hosts. The spontaneous development of a tumor is quite rare, but a change or variation in environment of the animal can induce many varied tumors. This variation of environment may be steroid treatment, irradiation, host-to-host serial transfer, tissue culture transfer, etc.<sup>1</sup> It is well known that there are "high tumor strains and low tumor strains" in many animal species. Contagion by contact with food, or animal or insect vectors is the usual method of spread of disease. Gross has termed this "horizontal" transmission of disease. In many diseases, there is another method of transmission from host to host usually from one generation to another, and this Gross termed vertical transmission.<sup>1</sup> For example: As far back as 1865, Pasteur observed that pebrine, a virus of the silkworm, was transmitted in insects through the eggs. Some virus mosaic diseases of plants, such as lettuce, tomato, etc., are not transmissible from hosts growing adjacently unless there is an intermediate carrier such as an insect. However, there seems to be a natural transmission of this mosaic virus through the seeds or tubers, and these viruses may at times remain dormant, not causing the disease unless activated in some way.<sup>1</sup> The Rocky Mountain rickettsiae are transmitted in the tic via the egg, from one generation to another, and are parasitic in these organisms, completely non-pathogenic to the tic. However, when transmitted to other species such as man, they are highly pathogenic. With these examples, it is obvious that this vertical spread of disease, when applied to human oncogenic virus, makes

study of this problem difficult. It is conceivable that the oncogenic virus or agent could be transmitted from parent to offspring via the germ cell and remain latent in the host until activated by other factors perhaps later in life. By the time of activation of this tumor agent, the host may have already transmitted the oncogenic potential to his offspring; and should this host die from other causes, then the "tumor" may have appeared to have skipped a generation. It is conceivable that this could go on for several generations, since the host would appear to be quite normal, and detection of this oncogenic virus be extremely difficult in the carrier host. The time factor in any epidemiological vertical transmission study in the human may be a tremendous obstacle. Certainly, among humans, records and descriptions of disease have not been carefully kept, nor was diagnosis made as absolutely, 100 years ago as it is today. Leukemia, of course, was only first recognized as a distinct human disease in the last century (1845). As stated before, the external factors (radiation, chemicals, irritants) that might trigger a latent oncogenic virus are many. Added to this variable are the known and unknown host factors (such as genetic makeup, metabolism, hormonal milieu, perhaps even the emotions) which make human research studies extremely difficult. With the above qualifications, epidemiological studies have been done. There have been many well known "cancer families" where members of the immediate and distant family in the same or succeeding generations have all had one or another form of malignancy. The similarity of malignant disease in animal and man from the epidemiological point of view has already been pointed out. Certainly leukemia in mice and humans is very similar both as to type, morphology, age of onset, etc. The leukemogenic virus of animals is an RNA virus, and therefore most of the human leukemia virus research has been focused on these viruses. The DNA type virus, many of which do not persist in the lesions they produce (e.g.; polyoma, adenopapilloma and SV40), has not been extensively studied.

Epidemiological studies of "clustering" or micro-epidemics of leukemia cases, suggest that some type of infectivity or perhaps increased susceptibility geographically occurs.<sup>28</sup> As has been stated before, virus type particles have been found in the plasmas of many of these patients included in these micro-epidemics (especially after concentration techniques in the plasmas), and some investigators are carefully studying family contacts and pets in these "epidemic" areas. While no significant conclusions can be drawn as yet, they potentially provide an additional lead in the study of the viral etiology of human tumors.

During the period 1959-1962, Dr. Denis Burkitt of Uganda, Africa, described a syndrome of a malignant lymphoma in African children now called the Burkitt or African lymphoma.<sup>29,30,31</sup> His fascinating epidemiological study seemed to determine a climatic limitation to the distribution of this disease. Most of these patients live within a geographic "belt," limited by altitude, temperature, rainfall, etc., and the suggestion has been made, though not substantiated, that this African lymphoma may well be transmitted by an insect vector, whose habitat is limited by similar geographic factors. The clinical syndrome, morphology both grossly and microscopically, etc., is a fairly consistent one. Recently however, similar type cases have been reported in the literature from other parts of the world, including the United States. O'Connor, et al, recently reported 20 cases selected from 148 cases of lymphoma in children, that were similar biologically and histologically to the Burkitt tumor.<sup>32</sup> He concludes that the "undue frequency of this lymphoma, which is comparatively uncommon in the U.S. . . its predilection for growth in the jaw and facial bones, which is even rarer in the United States, remain the only two important ways where this disease differs in the two geographic areas." However, these differences do exist, and certainly are factors which must be considered and studied further. Other laboratory studies may support a vector hypothesis. Banfield, et al, reported the transmission of a transplantable hamster lymphoma by mosquito, under experimental conditions.<sup>36</sup> This transfer seems to have occurred as a tumor cell transplant rather than of the original oncogenic agent or virus. There has also been reported (Balls) a spontaneous lymphoma in the African clawed frog which is probably viral-induced and possibly related to the Lucké frog carcinoma virus.<sup>33</sup> Electron microscopy morphology studies have suggested that the latter virus (Lucké) resembles the virus found in tissue cultures of Burkitt lymphoma cells.<sup>34</sup> As a result of this, several investigators are searching for possible amphibian reservoirs for the Burkitt lymphoma virus. It has been reported that Haddow, et al, have shown that mosquitos that feed on frogs also find man similarly appetizing.

The ability of several investigators to grow the Burkitt lymphoma in tissue culture, and the appearance of virus particles in some of these that are antigenically related to other human leukemia tissue culture lines, the ability of one investigator (Epstein) to produce a tumor resembling the Burkitt lymphoma in the African green monkey (after inoculating this monkey with material from the Burkitt lymphoma over a 2-year period) all point to this particular lymphoma and this area of study as promising leads.<sup>35</sup>



## Application To Therapy Of Human Tumors, Especially Leukemias

In spite of the above reported work, and much other work not reported in this paper, one is struck by the fact that we are just beginning in the human virus field. Gross isolated the first animal leukemia virus in 1951. In 1961, he made the following statement, which was essentially repeated by Rauscher in 1965, that "in spite of our considerable understanding of virus-induced tumors in animals we have yet to prevent or significantly modify the course of leukemia or lymphoma in any human patient with this type of information." Thus, the concerted and coordinated effort by leading centers throughout the country in this field, the development of techniques of growing human tumors, human tumor viruses, application of this to the development of a preventive or treatment vaccine or antiserum, the bio-assay of these, the bio-hazards of all of the above is the target of the recent government special Virus Leukemia Program.

All of us are aware of the variation in the course and the response of the human patient with malignant disease. The recent literature has been concerned with the factors of host resistance and the possible relationship between this and the immunologic response. The difficulties of working with human material are apparent and in spite of this even the newspapers have reported recent attempts at cross-tumor implantation in an attempt to induce increased host resistance or immunity. With our present ability to grow human tumor cells in tissue culture, work is now going on in many centers where these cells, free from the normal tissue and connective tissue, etc., that previously contaminated tumor antigens made from ground up surgical specimens are now being studied as to their possible use as immunizing agents or antiserum producing agents. These are the areas that are most promising in terms of the immediate application of presently known data to the therapy of human tumors.

There are still many fascinating unanswered questions. How does the virus actually change the cell to a tumor cell? Is the entire virus necessary or can a segment or RNA molecule from the virus produce the malignant change? Are there genetic differences that might be shown by chromosomal mapping in humans who develop malignant disease and those who do not? (There are certainly tumor resistant animal species.) If there are genetic differences that play a role in tumor resistance, would it be possible to manipulate or change the genetic makeup of the fetus or germ cell in this regard by as yet unknown physical or chemical techniques? The answer to any one of these might make a radical change in our therapeutic ability.

## Conclusion

If one can accept the overwhelming accumulated evidence that disease in man and other animal species is biologically similar, then we must accept the fact that as in animals, malignancy is viral induced. The exact nature and mechanism of induction is not yet known in either animal or man. The presence of an "activator" either of environmental or host origin is known to be present in both animals and man. The epidemiology of animal and human tumors, the clinical course and response to treatment and the recent demonstration in human tumors and human tumor tissue cultures of virus particles all support the theory of a viral etiology of human malignancy. We must await, however, the final definitive experimental data that will allow us to prevent or cure human malignancy. Until that time, we must utilize the information as a working theory and preliminary data, in our attempts to treat and further examine a very serious problem in the human as well as many other species.

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## COLON AND RECTAL QUESTIONNAIRE

Dr. N. William Wawro of Hartford wishes to express his thanks for the wonderful response of physicians in returning the American Cancer Society Colon and Rectal Questionnaire which was sent recently to all physicians. He requests that those who have not as yet participated in this study do so by sending in the desired information as soon as possible.



# ABO Blood Groups And Multiple Cancers

Zelda Janus, B.S., John C. Bailar, III, M.D., and Henry Eisenberg, M.D., M.P.H.

■ Many investigators have tried to find relationships between ABO blood groups and various diseases, including some forms of cancer. A report by Fadhli and Dominguez<sup>1</sup> showed an excess of blood group A among patients with multiple primary cancers of various sites when compared with a control population. The excess was statistically significant. Recently a study by Tsukada, et al<sup>2</sup> at Roswell Park Memorial Institute found no statistically significant differences in blood type between a multiple-cancer group and single-cancer group and between the multiple-cancer group and the normal population obtained from the literature. Our analysis is another attempt to confirm the findings of these studies.

The cancer patients in Table 1 are from a survey of hospitals and follow-up records of 5,366 patients with malignant tumors of the uterine cervix and corpus. The series includes all Connecticut residents known to have a first diagnosis of uterine cancer from 1935 to 1951 and who were admitted to hospitals. Three hundred sixty-two of these patients also had malignant tumors of other sites before, simultaneously with, or after the uterine cancer.<sup>3</sup> Table 1 also shows the distribution of blood group in three control series. The control series contain persons of both sexes and probably younger people than in the study, but there is no evidence to indicate that age or sex has an effect on blood type distribution.

Chi-square tests were applied to the data in Table I to see if patients with single or multiple tumors had distributions of blood groups which differed significantly from the control series. In computing chi-square, blood groups B and AB were considered as a single group. The results of these chi-square tests are given in Table II. Significant differences were found between blood groups of the various control populations and patients with *single* cancers of the corpus uteri but not for multiple cancers. These data therefore do not support the observation of Fadhli and Dominguez with respect to the blood group distribution of patients with multiple tumors. These results tend to agree with Tsukada, et al who do not feel that they have

established a clear relationship between blood type and the occurrence of multiple cancers.

Two limitations on the present series must be noted. First, blood group was determined for less than half of the patients in the original cancer series (170 of 362 patients with multiple cancer and 1804 of 5004 with single cancers). The incomplete data reduces the effective sample size but it is difficult to see how it could introduce any appreciable bias in the results. Second, every patient in the series had one cancer in the uterine cervix or corpus. The other studies do not give blood group distribution for specific sites of cancer in their series; it is possible that there is a relationship existing between blood group and multiple cancers in pairs of sites which do not include uterus, such as skin-breast or lung-rectum.

## Summary

The distribution of ABO blood groups of 170 cases of multiple primary cancers, all of which included uterine cervix or corpus as one site, was compared with the distribution in three different control groups and with that for 1804 cases of single cancer in the cervix or corpus. The blood group distribution of patients with multiple cancers was not found to differ significantly from either the distribution in patients with single cancer or the control distributions.

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TABLE I  
ABO BLOOD GROUPS FOR PATIENTS WITH MULTIPLE PRIMARY  
CANCERS OR SINGLE UTERINE CANCERS AND FOR CONTROL GROUPS

|                                               | NUMBERS |     |     |     |    |              | PERCENT DISTRIBUTION OF PATIENTS<br>WITH KNOWN BLOOD GROUPS |      |      |      |     |
|-----------------------------------------------|---------|-----|-----|-----|----|--------------|-------------------------------------------------------------|------|------|------|-----|
|                                               | TOTAL   | O   | A   | B   | AB | UN-<br>KNOWN | TOTAL                                                       | O    | A    | B    | AB  |
|                                               |         |     |     |     |    |              |                                                             |      |      |      |     |
| <i>Multiple primary tumors</i>                |         |     |     |     |    |              |                                                             |      |      |      |     |
| Cervix                                        | 163     | 27  | 31  | 10  | 1  | 94           | 100.0                                                       | 39.1 | 44.9 | 14.5 | 1.5 |
| Corpus                                        | 199     | 42  | 40  | 14  | 5  | 98           | 100.0                                                       | 41.6 | 39.6 | 13.9 | 4.9 |
| Total                                         | 362     | 69  | 71  | 24  | 6  | 192          | 100.0                                                       | 40.6 | 41.8 | 14.1 | 3.5 |
| <i>Single uterine cancers only</i>            |         |     |     |     |    |              |                                                             |      |      |      |     |
| Cervix                                        | 2845    | 446 | 368 | 112 | 33 | 1886         | 100.0                                                       | 46.5 | 38.4 | 11.7 | 3.4 |
| Corpus                                        | 2159    | 415 | 309 | 100 | 21 | 1314         | 100.0                                                       | 49.1 | 36.6 | 11.8 | 2.5 |
| Total                                         | 5004    | 861 | 677 | 212 | 54 | 3200         | 100.0                                                       | 47.7 | 37.5 | 11.8 | 3.0 |
| <i>Control groups</i>                         |         |     |     |     |    |              |                                                             |      |      |      |     |
| A. Fadhli & Dominguez <sup>1</sup>            | XX      | XX  | XX  | XX  | XX | XX           | 100.0                                                       | 44.9 | 41.0 | 10.3 | 3.8 |
| B. Nat'l Blood Donor <sup>2</sup>             | XX      | XX  | XX  | XX  | XX | XX           | 100.0                                                       | 45.5 | 40.8 | 10.0 | 3.7 |
| C. Conn.Red Cross<br>Blood Donor <sup>2</sup> | XX      | XX  | XX  | XX  | XX | XX           | 100.0                                                       | 43.7 | 40.3 | 11.7 | 4.3 |

<sup>1</sup> Weighted average of 5 series given by Fadhli and Dominguez

<sup>2</sup> Eisenberg, et al. (4).

TABLE II  
CHI-SQUARE VALUES FOR COMPARING BLOOD GROUP DISTRIBUTION

|                                                        | TOTAL ONE SITE<br>EITHER IN<br>CERVIX OR CORPUS | ONE SITE<br>IN<br>CERVIX | ONE SITE<br>IN<br>CORPUS |
|--------------------------------------------------------|-------------------------------------------------|--------------------------|--------------------------|
| Multiple primary cancers versus single uterine cancers | 3.29                                            | 1.48                     | 2.54                     |
| Multiple primary cancers versus control A              | 2.24                                            | .94                      | 1.89                     |
| Multiple primary cancers versus control B              | 2.92                                            | 1.18                     | 2.32                     |
| Multiple primary cancers versus control C              | .76                                             | .70                      | .62                      |
| Single uterine cancers versus control A                | 9.05 <sup>a</sup>                               | 2.87                     | 7.42 <sup>a</sup>        |
| Single uterine cancers versus control B                | 8.02 <sup>a</sup>                               | 3.00                     | 6.27 <sup>a</sup>        |
| Single uterine cancers versus control C                | 11.85 <sup>a</sup>                              | 3.05                     | 10.04 <sup>a</sup>       |

<sup>a</sup> Significant at P = .05 level with 2 degrees of freedom.



# Carcinoma Of The Cervix

John McLean Morris, M.D.

■ Just over a hundred years ago Charles D. Meigs of Philadelphia, Professor of Midwifery and the Diseases of Women and Children, wrote, "It is enough to make a physician's heart sink within him to make the diagnostic of cancer uteri, for such a diagnosis is *ipso facto* a prognostic of death; and when the physician has made it, and is brought to the point of giving true expression to his opinion, he might be supposed to be as painfully situated as the judge on the bench, when he puts on his black cap before the final announcement of the judgment unto death." While the late Ferderick D. Irving, Professor of Obstetrics at Harvard, once referred to this learned Philadelphia professor as "a barnacle of the ship of progress," the observations expressed in the quotation above represented the contemporary view in 1850.

Cure rates in cancer of the cervix since 1900 have roughly approximated the year of the century. Originally most of the progress was the addition of surgery and radiotherapy as treatment modalities. More recently, at least 75 per cent of the improvement in cure rates is due to earlier diagnosis. Today approximately 8 out of 10 women with early cervical cancer can anticipate cure.

## Epidemiology

It has long been known that cancer of the cervix has an association with early marriage, multiparity, and poor hygiene (Table I). Epidermoid carcinoma of the cervix is more common in lower economic groups, less common in groups in which ritual circumcision is performed, and almost non-existent in virgins. As smegma has been shown to be car-

TABLE I  
CARCINOMA OF CERVIX  
Factors Related to Incidence  
(Expressed in per cent)

|                                  | CARCINOMA<br>OF CERVIX | CARCINOMA<br>OF BREAST | GENERAL<br>POPULATION |
|----------------------------------|------------------------|------------------------|-----------------------|
| Marriage before the<br>age of 20 | 45.5                   | 16.2                   | 18.6                  |
| Marriage at any age              | 96.9                   | 83.5                   | 83.2                  |
| Parity                           | 87.2                   | 68.0                   | 68.9                  |
| Syphilis                         | 8.4                    | 2.2                    |                       |

(Figures from Massachusetts Department of Public Health)

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cinogenic, this evidence suggests that prolonged periods of intercourse with uncircumcized males of poor penile hygiene may be an etiologic factor in the disease.

Figures from the Connecticut State Tumor Registry (Table II) show that this disease has an extremely long life history with a median of 7.9 years between development of carcinoma in-situ and development of invasive carcinoma, and a median of 8.5 years between local invasive carcinoma and distant metastases.<sup>2</sup> As it is generally recognized that cervical dysplasia may precede carcinoma in-situ, the total period of development of the disease may be even longer.

TABLE II  
CERVICAL CANCER IN CONNECTICUT  
1935-1951

|                | NO. OF CASES | MEDIAN AGE |
|----------------|--------------|------------|
| In-situ        | 165          | 42.8       |
| Localized      | 1,488        | 50.7       |
| Regional       | 1,232        | 54.2       |
| Distant        | 218          | 59.2       |
| (Stage unknown | 70)          |            |
| All cases      | 3,173        | 52.2       |

Carcinoma of the cervix should be to some extent a preventable disease. The decreasing incidence noted in some areas may be related to better hygiene, routine circumcision of the male, the use of birth control techniques in reducing grand multiparity, detection and recognition of the disease in the preinvasive stages, and the performance of total rather than subtotal hysterectomy. In past years approximately 10 per cent of the patients with cervical cancer seen at Yale-New Haven Medical Center have been cervical stump cases.

The age specific incidence of this disease (Table III) should be considered in planning cytologic screening programs. In terms of maximum utilization of medical and scientific manpower, routine smears in patients under twenty yield only one case

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TABLE III  
CARCINOMA OF THE CERVIX  
INCIDENCE AND AGE SPECIFIC INCIDENCE PER 100,000  
CONNECTICUT 1935-1951

| AGE       | NO. OF CASES | AGE SPECIFIC<br>INCIDENCE |
|-----------|--------------|---------------------------|
| 15-19     | 2            | .15                       |
| 20-24     | 12           | .9                        |
| 25-29     | 64           | 4.8                       |
| 30-34     | 155          | 12.0                      |
| 35-39     | 303          | 24.9                      |
| 40-44     | 482          | 44.1                      |
| 45-49     | 479          | 46.2                      |
| 50-54     | 439          | 47.3                      |
| 55-59     | 439          | 56.5                      |
| 60-64     | 379          | 56.6                      |
| 65-69     | 270          | 50.1                      |
| 70-74     | 167          | 44.5                      |
| 74-79     | 97           | 39.9                      |
| 80-84     | 50           | 40.3                      |
| 85 & over | 24           | 38.5                      |
| Total     | 3,378        | 21.6 per 100,000          |

per 1,000,000 women; in patients under 25 only one per 100,000 (Table III). In this group smears should be limited to those who have suspicious areas on the cervix. Most screening programs yield roughly 5 abnormal smears per 1,000 on the initial visit, which rapidly falls off to a tenth of this figure in succeeding years. These figures are roughly what might be expected. If 50 women per 100,000 are to develop cancer of the cervix per year, and the disease has a 10-year life span, one would expect to find 500 abnormalities per 100,000 in initial sampling. If 10 per cent false negatives are encountered, 5 of these women would receive false reassurance.

### Diagnosis

The diagnosis of cervical cancer belongs in the hands of any physician, surgeon, or gynecologist who sees a woman in the cancer age. Routine use of the Papanicolaou smear in patients over the age of 25, the annual check-up, the performance of pelvic examinations at the time of hospital admissions and office visits have played important roles in earlier diagnosis. While there have been a certain number of experimental screening studies carried out in which "do it yourself kits" have been provided for women to take their own smears, there are a good many reasons for regarding such a program with disfavor. The cytologic smear is only one of the many tests for diagnosing pelvic cancer, and not only false negatives, but also the inability of the smear to detect other pelvic pathology, may provide false reassurances for the patient.

The decision as to what course to take in the event of a suspicious or positive smear does not lend itself to a single answer. Some authorities, in an effort to provide such an easy answer, advise immediate conization. A routine cervical conization as an initial procedure has the disadvantages of the expense of hospitalization, the risk of anesthesia, and the traumatic psychologic effect on the patient. The operation is not simple and without complications. Hemorrhage or infection (especially if cautery is used) not only relate to the procedure itself, but also to any subsequent therapy which may be undertaken. Doran and Shier<sup>7</sup> report 22 per cent significant complications from conization, as well as a 45 per cent morbidity following subsequent hysterectomy. Laubach and McGinty<sup>13</sup> note the morbidity in hysterectomy post-cone increased to 54.6 per cent. Kottmeier<sup>12</sup> reports 50 per cent of patients coned aborted when they became pregnant. Other reports indicate similar results, especially during pregnancy (Table IV). Furthermore, unless a cone is carefully cut, fragments of un-oriented tissue, particularly if cauterized or inadequately sectioned, may prove of less value than carefully chosen punch biopsies.

When an unsuspected suspicious or positive smear is reported, a repeat smear should be routine. Because of the unnecessary anguish caused by a false positive, it is probably wiser not to tell the patient she has a positive smear for cancer, but merely that the smear must be repeated. The surface of the cervix can be stained with Lugol's solution and non-staining areas biopsied. Toluidine blue, Schiller's solution, colposcopy or other techniques may be employed. Significant exocervical growth is usually recognizable. The major danger is unrecognized endocervical tumor. For this pur-

TABLE IV  
CONIZATION FOR POSITIVE CYTOLOGY DURING PREGNANCY

| AUTHOR                          | NO. OF CASES | SE-<br>VERE<br>HEMOR-<br>RHAGE* | OR<br>PRE-<br>MATU-<br>RITY | FETAL<br>LOSS** | INVASIVE CANCER  |
|---------------------------------|--------------|---------------------------------|-----------------------------|-----------------|------------------|
|                                 |              |                                 |                             |                 |                  |
| Beecham and Andros <sup>1</sup> | 26           | 2                               | 1                           | 0               | 2                |
| Ferguson and Brown <sup>8</sup> | 50           | 6                               | 16                          | 6               | 5                |
| Dean et al. <sup>6</sup>        | 39           | 1                               | 6                           | 2               | 2 (micro)        |
| Moore et al. <sup>14</sup>      | 14           | 0                               | 1                           | 0               | 5 (4 micro)      |
|                                 | 129          | 9                               | 24                          | 8               | 14 (? no. micro) |

\* Requiring readmission and transfusion (1 infarct, 1 anuria).

\*\* Excluding loss from therapy of cervical lesion.



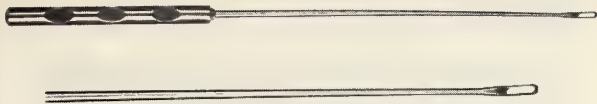


FIG. I. Endocervical Curette.

pose a small endocervical curette is of great value (Fig. I). This technique is used routinely in our clinic. Many of our endometrial cancers are similarly diagnosed with a Meigs endometrial biopsy curette prior to hospital admission. Approximately 90 to 95 per cent of cervical cancer can be diagnosed by office procedure.

Should punch biopsies be equivocal, the procedure of choice is a cone with immediate cryostat sections taken in the operating room and appropriate treatment instituted under the same anesthesia.<sup>11</sup> It is preferable to suture such a coned area than to cauterize it, and the report from the sections should be available at about the time the suturing is completed.

Pathology

The first step in proper handling of cervical malignant disease is the review of the pathologic material available. It must be determined whether it is representative and adequate. Many times lesions are borderline. It is not correct to assume in all cases that it is black or white, cancer or benign. Severe dysplasias should at times be treated as premalignant lesions. Micro-invasive tumors do not necessarily require as rigorous treatment as Stage I cancer.

It should be stressed in regard to cervical conization that many of the so-called invasive carcinomas picked up by this technique are in fact micro-invasive carcinomas. We have used this term to refer to tumors that are not grossly visible to the naked eye in which the depth of penetration of invasion is not more than 3 mm. In our experience such tumors have essentially the same prognosis and significance as carcinoma in-situ, unless the histology is most unusual with lymphatic involvement and severe anaplasia.

On the other hand, a severe dysplasia should be recognized as a premalignant lesion. While such lesions undoubtedly have less significance than carcinoma in-situ, over a long term many of these will actually progress into carcinoma in-situ or invasive tumors.

There is also little question that tumors with extensive lymphatic involvement, diffuse cellular infiltration of tissues, or very marked anaplasia have a worse prognosis than well differentiated tumors with more sharply demarcated borders.

TABLE V  
PAIN IN CERVICAL CANCER  
(262 cases 1952-1958)

| LOCATION OF PAIN      | NO. OF<br>CASES | 3-8 YR. | 3-8 YR.     |
|-----------------------|-----------------|---------|-------------|
|                       |                 | "CURES" | "CURE" RATE |
| No pain               | 120             | 97      | 81 %        |
| Abdomen, pelvis, back | 65              | 36      | 55.4%       |
| Hip                   | 12              | 3       | 25 %        |
| Thigh                 | 65              | 8       | 12.3%       |

Individuals who assume the responsibility of caring for patients with such lesions or with invasive cancer should become sufficiently familiar with the pathologic processes involved that they can intelligently review the slides themselves, and apply this knowledge to the patient in relation to childbearing and the many other situations that may be a part of the problem.

Extent Of Disease

The control of the primary disease in the cervix does not present the major problem in therapy—it is the extension to other pelvic structures that presents difficulties. Pain, especially if involving the leg, or ureteral obstruction may indicate pelvic wall extension. The impact of these on prognosis can be seen in Tables V and VI. It is unfortunate that ureteral obstruction is not considered in clinical staging, as involvement of the ureter, even if not palpable, makes a case the equivalent of a Stage III or IV from the prognostic point of view.

In addition to the intravenous pyelogram, diagnostic procedures should include cystoscopy and metastatic series. Sigmoidoscopy is usually unnecessary. Venography and lymphangiography are tedious to perform, uncomfortable to the patient, and

TABLE VI  
URETERAL OBSTRUCTION IN CARCINOMA OF THE CERVIX  
1952-1958

| STAGE              | NO. OF<br>CASES | PRI-<br>MARY<br>URE-<br>TERAL<br>OB-<br>STRU- | SECON-<br>DARY<br>URE-<br>TERAL<br>OB-<br>STRU- | TOTAL NO. |      | %<br>/o |
|--------------------|-----------------|-----------------------------------------------|-------------------------------------------------|-----------|------|---------|
|                    |                 | TION                                          | TION                                            | NO.       | DIED |         |
| I                  | 103             | 1                                             | 9                                               | 10        | 10   |         |
| IIA                | 53              | 0                                             | 8                                               | 8         | 8    |         |
| IIB                | 30              | 2                                             | 9                                               | 11        | 11   |         |
| III                | 19              | 7                                             | 5                                               | 12        | 10   |         |
| IV                 | 23              | 12                                            | 3                                               | 15        | 13   |         |
| Total              | 228             | 22                                            | 34                                              | 56        | 52   | 92.9    |
| Recurrent<br>Cases | 34              | 15                                            | 2                                               | 17        | 12   |         |
| Total              | 262             | 37                                            | 36                                              | 73        | 64   | 87.7    |

may have undesirable side effects. The results may be equivocal, and in most circumstances would not significantly alter the treatment. While sometimes of value in the unusual situation or as an experimental procedure, they are undesirable for routine use.

Treatment

The position of treatment in cancer of the cervix has been the subject of much feeling debate and conflicting statistical reports to justify the particular stand taken. Participants and discussors alike may be confused by use of 5-year survival statistics collected by a variety of methods—many of which are statistically unsound and do not take into consideration the selection of cases involved. As different specialties are involved often the decision is made by an individual who is actually not familiar with the details of other modalities of treatment. The ideal therapist is one who is acquainted with all of these.

Carcinoma in-situ is best treated by total hysterectomy. It should be remembered that this is a preinvasive process with a considerable length of time elapsing before significant invasion occurs. There is no urgency about the operative treatment. A pregnant patient should be permitted to go to term with operation performed some weeks after vaginal delivery. While a cone may aid in the diagnosis, except in the earliest type of premalignant change, a cone is not sufficient treatment in itself. Kottmeier<sup>12</sup> reports 8 coned patients with carcinoma in-situ who later developed cervical carcinoma.

In our experience the micro-invasive tumor can be treated similarly by wide hysterectomy. Although node dissection was carried out, in a limited series of these cases no positive nodes were encountered. There has been no tumor recurrences in this series.

Other than carcinoma in-situ or the micro-invasive tumor the treatment of cervical cancer more properly belongs to a therapy center. The care of the patient with carcinoma of the cervix requires considerable experience and individualization of treatment. No matter how well trained a physician may be, unless he is in constant contact with such problems he cannot maintain the skills required in a specialized area which is constantly changing. Figures from New York State<sup>9</sup> show that results

TABLE VII  
5-YEAR SURVIVAL RATES RELATED TO TYPE OF HOSPITAL  
NEW YORK STATE, 1949<sup>9</sup>

| STAGE                       | I    | II-IV | TOTAL |
|-----------------------------|------|-------|-------|
| Cancer & Teaching Hospitals | 67.6 | 36.2  | 50.7  |
| Non-teaching Hospitals      | 42.8 | 12.4  | 30.5  |

TABLE VIII  
5-YEAR SURVIVAL RATES RELATED TO HOSPITAL SIZE  
CONNECTICUT 1935-51<sup>3</sup>

| STAGE                          | FEWER THAN<br>350 BEDS | MORE THAN<br>350 BEDS |
|--------------------------------|------------------------|-----------------------|
| Confined to cervix             | 60                     | 64                    |
| Regional extension             | 26                     | 41                    |
| Remote extension or metastases | 12                     | 20                    |

from cancer and teaching hospitals were significantly better than from nonteaching hospitals (Table VII). Figures from the Connecticut State Tumor Registry<sup>3</sup> related to hospital size show similar results, especially in tumors with regional extension (Table VIII). The doctor in private practice who ignores these results and undertakes treatment himself is simply not giving his patient the best that is available to her.

The radiotherapy technique employed at Yale Medical Center is described elsewhere.<sup>15</sup> Radium applications are done with flexible rubber applicators fitted to the surface of the tumor using a scintillation counter to obtain rectal and bladder dose readings. Satisfactory treatment of the pelvic wall is best done with supervoltage therapy. The major principles involve the administration of a tumoricidal dose to the involved areas, recognizing that the mucosa of rectum, bladder, sigmoid, and small bowel must be spared this same dose in order to avoid injury. There is evidence in some cases that the primary tumor must receive a higher dose than is perhaps necessary for nodal or other spread.

Primary surgery in selected cases offers cure rates roughly equal to those achieved by radiotherapy, but, (1) radical surgery is difficult and beyond the competence of the average obstetrician-gynecologist, (2) the morbidity, especially urinary fistula, is higher than that of good radiotherapy, (3) if surgery fails, it is hard to carry out satisfactory radiotherapy (in the absence of the uterus to hold radium), whereas if radiotherapy fails, surgery may be performed as a secondary procedure (assuming tissue tolerances have not been exceeded). Surgical cures in radiation failures may be as high as 20 per cent.

Cases selected for primary surgery usually are early cases in young women who are good surgical risks. The fact that elderly patients, poor surgical risks, and advanced tumors are usually turned over to radiotherapy weights results in favor of most surgical series. An exception to this are the advanced Stage IV cases, particularly when the tumor has extended anteriorly and posteriorly to the bladder and rectum without extension to the pelvic wall. In these patients pelvic exenteration procedures may offer surprisingly good results in terms of cure.



However, because of the mutilating nature of such surgery and the late renal difficulties and other problems that can be anticipated in a high proportion of such cases, exenterative procedures have been limited in our hands to (1) post-radiation cases in which there is no other alternative of therapy and (2) those in which there is reasonable hope of cure. In only rare instances can the operation be considered palliative.

Routine combinations of the two modalities of therapy are ill-advised and in general only serve to increase morbidity without significantly improving results. However, surgery in the case of suspected recurrence may have a place.

In such circumstances one of five situations may arise:

- 1) The patient succumbs to surgery.
- 2) No tumor is found.
- 3) Inoperable tumor is found.
- 4) The tumor is removed, but recurs.
- 5) The tumor is removed and the patient remains cured.

In most circumstances only No. 5 can be considered to be of benefit to the patient. This occurs more commonly in low-grade tumors, and it must be recognized that some patients may survive for 5 years without surgery. (e.g. F.T. #BO-91-20. Cervical carcinoma treated 1942, one positive inguinal node removed at 5 years, two positive iliac nodes removed at 10 years, has now survived 12 more years without evidence of disease.)

To put such a question as post-radiation lymph node dissection into a simple formula let:

- a = per cent cases with residual operable tumor
- b = per cent 5 yr. survival if tumor present and removed
- c = per cent 5 yr. survival if tumor present and not removed
- d = operative mortality

then if  $(a \times b) - (c + d) = 0$  or less, no benefit is to be anticipated from this surgery. For example, if  $a = 20\%$ ,  $b = 20\%$ ,  $c = 1\%$ ,  $d = 3\%$   $(.20 \times .20) - (.01 + .03) = .04 - .04 = 0$ . Under such circumstances not only is there no statistical benefit from the surgery, but unfortunately most of the operative mortality occurs in patients who had no disease. Furthermore, this does not take into consideration such matters as operative morbidity, including lymphocysts, ureteral injury, or other difficulties which may in themselves prove incapacitating or even eventually fatal.

While local recurrence proven by biopsy should be an indication for surgical intervention, the most common sign—one with an ominous prognosis—is pain. In such instances, intravenous pyelogram

showing the appearance of ureteral obstruction may generally be considered a pathognomonic sign. If the pain involves the thigh, particularly if leg swelling is present, the prognosis is essentially hopeless. Metastatic series, liver scan and function tests, and neurologic evaluation may be of some value in determining the extent and location of the disease.

Some palliation may be achieved by a variety of methods:

- 1) systematic chemotherapy
  - 2) local chemotherapy infusion or perfusion
  - 3) laparotomy and radiocolloidal gold injection<sup>17</sup>
  - 4) cordotomy, nerve root section, or lobotomy
- Rarely is re-irradiation indicated if the original radiotherapy was adequate, as this only increases injury without improving the patient's lot. Occasionally radiation of an affected area outside the original treatment site may be of benefit in palliation of local symptoms.

### Results

The Annual Reports on Results of Treatment published in Stockholm<sup>1</sup> have done much to standardize techniques of reporting so as to make comparable statistics available. There are still many local undetermined variables, such as pathologic interpretation as to what constitutes invasive tumor, conscious or unconscious factors in selection of cases, and particularly variations in interpretation of staging, all of which should be taken into account when comparing results.

Staging represents a clinical impression. The determination of early extension in the fornices or parametrial areas, and the evaluation of such matters as "paracervical thickening" or "bands," is a matter of interpretation which may lead to considerable variation in the assignment of cases to clinical stages, especially I and III (Stage II only reflecting the cases not assigned to I and III). If the type of clinical material seen in two institutions is similar, the institution placing only a small proportion of cases in Stage I and a high proportion in Stage III will show a higher cure rate in each stage than an institution placing a high proportion of cases in Stage I and low proportion in Stage III.

If the clinical material seen in most centers in the United States and Canada may be assumed to be roughly equivalent, it is interesting to make a comparison between the two institutions in the Annual Reports that report less than 15 per cent of their cases in Stage I and more than 40 per cent in Stage III with the seven institutions reporting more than 40 per cent in Stage I and less than 15

TABLE IX

CARCINOMA OF THE CERVIX (FROM ANNUAL REPORT)<sup>1</sup> 1953-1957

| STAGE | TWO INSTITUTIONS*         |                             | SEVEN INSTITUTIONS**      |                             |
|-------|---------------------------|-----------------------------|---------------------------|-----------------------------|
|       | (U.S.A. & CANADA)         |                             | (U.S.A. & CANADA)         |                             |
|       | PER CENT OF PTS. IN STAGE | AVERAGE OF 5-YR. CURE RATES | PER CENT OF PTS. IN STAGE | AVERAGE OF 5-YR. CURE RATES |
| I     | >15%<br>(13.7-13.9)       | 87.4                        | >40%<br>(43.2-61.2)       | 74.7                        |
| II    |                           | 63.1                        |                           | 46.3                        |
| III   | <40%<br>(42.3-59.5)       | 44.1                        | <15%<br>(8.2-14.4)        | 23.9                        |
| IV    |                           | 13.8                        |                           | 11.2                        |
| I-IV  |                           | 53.5                        |                           | 54.0                        |

\* M. D. Anderson, Ellis Fischel.

\*\* Yale, Cornell, California, Pennsylvania, Woman's Inst. Cancer Royal Victoria.

per cent in Stage III (Table IX). Although the overall cure rate is similar in the two groups, the cure rate by stages is considerably better in the first. While some of this may be due to a different type of case that is being seen, the interpretation of staging may also play a role.

In Table X Yale-New Haven Medical Center is compared with the 115 reporting institutions in the International Reports. Of these 115 institutions, only one institution has a lower proportion of patients in Stage III. This would suggest that either an earlier type of case is being seen here than in other institutions, or, more likely, the matter of fixation to the pelvic wall in Stage III has been interpreted in too rigid a fashion, and that some of the cases with bands extending to the pelvic wall which have been classed as I or II should have been classified as Stage III. Some of the poor results in Stage III may also be laid to the fact that there was a lag in obtaining supervoltage therapy which is an integral part of Stage III therapy.

### Complications

Cure rates are not the only measure of success or failure of a modality of therapy. Complications may be more of a burden to the patient than the disease itself. An exenteration may prove curative in carcinoma *in situ* of the cervix but it may not in the long run be in the best interest of the patient. Enthusiasm for new supervoltage techniques, radical surgical procedures, or combinations thereof, may prevent the gynecologist from recognizing that the same or better results could have been achieved by simpler means. Programs advocating massive pelvic radiation or routine combinations of extensive radiation and radical surgery sometimes ignore complications.

Radiologic injuries are largely related to the fact that the mucosa of bowel and bladder may be seriously damaged by a tumoricidal dose of radiation. Extreme care must be taken to avoid injury to these structures, including direct measurements from rectum and bladder at the time of radium implantation.

Primary surgery is associated with a higher percentage of injury than is usually encountered with good radiation therapy. Brunschwig and Barber<sup>5</sup> recently reported a surgical series in which 22 per cent of the patients developed urinary tract fistulas (excluding exenteration cases). In our series the combination of surgery and radiation resulted in a complication rate which was over three times greater than that of patients receiving radiation alone.<sup>10</sup> While two-thirds of the radiation injuries were transient, when surgery was added two-thirds of the injuries were permanent or required surgical intervention. Any combination of these two modalities should be undertaken with great care and with recognition of the risks involved to the patient.

### Conclusion

The proper handling of cervical cancer involves the knowledge of a variety of specialties including pathology, gynecology, urology, radiotherapy, general surgery, and chemotherapy. This may be handled by a multidisciplinary approach using separate services. It is more satisfactory usually from a patient's point of view if the gynecologic oncologist familiarizes himself with all of these areas, using consultants if and when necessary. Without good cooperation the patient invariably suffers or "falls between the cracks" with no one doctor assuming the real responsibility.

Surgery in the radiated pelvis presents very different healing problems from the non-radiated pelvis. Similarly, primary surgery may make later radiotherapy difficult or impossible, particularly radium insertion. Chemotherapy may be affected by prior radiation treatment. The frequent involvement of bladder, ureters, bowel, pelvic nodes, nerves, and

TABLE X

CARCINOMA OF THE CERVIX (FROM ANNUAL REPORT)<sup>1</sup> 1953-1957

| STAGE | 115 REPORTING INSTITUTIONS |                          | YALE-NEW HAVEN MEDICAL CENTER |                          |
|-------|----------------------------|--------------------------|-------------------------------|--------------------------|
|       | PER CENT OF PTS. IN STAGE  | 5-YR. APPARENT CURE RATE | PER CENT OF PTS. IN STAGE     | 5-YR. APPARENT CURE RATE |
|       |                            |                          |                               |                          |
| I     | 24.6                       | 74.9                     | 44.1                          | 78.7                     |
| II    | 37.8                       | 53.0                     | 37.1                          | 54.0                     |
| III   | 31.8                       | 30.2                     | 8.2                           | 21.7                     |
| IV    | 5.8                        | 8.1                      | 10.6                          | 11.1                     |
| I-IV  | 100                        | 48.5                     | 100                           | 57.6                     |



vessels makes more knowledge of general and urologic survey necessary than is included in the ordinary obstetrical and gynecologic training. Regional surgical knowledge in the pelvis has an advantage over organ specialization; knowledge of the disease and its treatment is preferable to separating modalities of therapy.

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# Experience With Salivary Gland Tumors At Hartford Hospital 1936-1963

N. William Wawro, M.D. and Philip Becker, M.D.

■ The most common cause for unilateral, painless, progressive swelling or mass in the preauricular or submaxillary triangle is a primary tumor of salivary gland origin. If facial nerve weakness, local pain, or ipsilateral cervical lymph node enlargement are associated with such a preauricular or submaxillary mass, the probability of a malignant tumor of major salivary gland is great and requires immediate attention. Most tumors of major salivary gland origin are benign with the highest incidence in adults, though large cavernous hemangiomas may be found in the parotid salivary gland of the newborn infant.

It is not commonly realized that salivary gland tissue is present within the mucosa of the buccal, palatine and base of tongue areas. This heterotopic salivary gland tissue can give rise to primary salivary gland tumors, generally malignant and commonly of the cylindroma (low grade adenocarcinoma) variety. It should be noted that these minor salivary gland tumors differ from the more common intra-oral squamous carcinomas in that they appear initially as submucosal nodules which slowly increase in size and ulcerate only in the late and advanced stages. The general rule that there is an increasing likelihood of malignancy as one progresses from parotid to submaxillary to sublingual in the oral naso-pharyngeal areas is a diagnostic clue well worth remembering.

Because the facial nerve traverses the quite vascular and saliva secreting parotid gland, many patients with parotid tumors have been advised to defer treatment until the parotid mass causes "trouble" or "ripens." The spectre of severing or damaging the seventh cranial nerve in its course through the parotid gland with resultant facial paralysis, or creating a permanent salivary cervical fistula by incising the parotid, have been fears which often delay prompt and appropriate action for primary parotid salivary gland tumors.

These fears are groundless. Subtotal resection of the parotid gland can be carried out without facial nerve injury or salivary fistula by removing the entire superficial lobe with controlled exposure of the facial nerve and ligation of Stenson's duct. In this

series of 62 consecutive subtotal resections for benign parotid tumors, there was no single salivary oro-cervical fistula or facial nerve section.

There is little doubt that the best control and survival of both benign and malignant salivary gland tumors is achieved with adequate and prompt surgical therapy. In the era before World War II, excision of these neoplasms with limited margins or excision biopsy of a portion of the salivary gland tumor was commonly practiced. With benign tumors, local recurrence was expected and generally treated with another limited excision or supplementary X-ray therapy.

If the salivary gland tumor was malignant, X-ray therapy or interstitial radiation was employed with limited success and low survival rate, since these patients succumbed to a combination of locally invasive recurrence and disseminated metastases.

## Material

This study covers the experience at the Hartford Hospital for 26 years, 1936-1963, during which time a total of 290 primary neoplasms of major and minor salivary gland origin were recorded and treated. Long term followup is available on 242 of the 290 patients, followed well over ten years. (83 per cent). In 214 patients the tumors were benign (74 per cent) and in 76 patients (26 per cent), the tumors were malignant histologically. (Table I). The latter group contains the less aggressive cylindromata (adenocystic-adenocarcinoma and mucoepidermoid carcinoma) which have a slow growth rate, and infrequently metastasize to the regional cervical lymph nodes as well as the more aggressive, highly malignant squamous and undifferentiated carcinoma which have a rapid growth rate, with a higher incidence of cervical lymph node and hematogenous metastases. The average age in this series for benign and malignant tumors is 56 years of age, and except for a male dominant in the Warthin's tumor, and female dominant in the malignant cylindromas, the remaining groups were evenly distributed. (Table II).

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TABLE I  
HARTFORD HOSPITAL  
1936-1963

| CLASSIFICATION                 | SUBMAXIL- |      |       | TOTAL |
|--------------------------------|-----------|------|-------|-------|
|                                | PAROTID   | LARY | OTHER |       |
| Benign                         |           |      |       |       |
| Mixed tumor                    | 152       | 21   | 8     | 181   |
| Adenolymphoma ,<br>(Warthin's) | 17        | 0    | 1     | 18    |
| Cavernous hemangioma           | 15        | 0    | 0     | 15    |
|                                | 184       | 21   | 9     | 214   |
| Malignant                      |           |      |       |       |
| Cylindroma                     | 15        | 3    | 4     | 22    |
| Muco-epidermoid                | 15        | 0    | 0     | 15    |
| Adenocarcinoma                 | 12        | 2    | 1     | 15    |
| Squamous carcinoma             | 16        | 2    | 0     | 18    |
| Undiff. carcinoma              | 5         | 1    | 0     | 6     |
|                                | 63        | 8    | 5     | 76    |
| Total                          | 247       | 29   | 14    | 290   |

### Diagnosis

As a general rule, parotid enlargement is either localized or diffuse. Localized parotid swelling most likely represents a primary benign or malignant parotid neoplasm, if the patient has not had a previous excision of a primary facial skin epithelioma or melanoma. Intra-parotid lymph nodes may become enlarged with metastatic cancer from primary head or facial skin cancer several years later, despite control of the former skin neoplasm.

Occasionally, a primary parotid mixed tumor may arise in the smaller deep retromandibular lobe and present as a lateral pharyngeal, retrotonsillar submucosal firm mass without swelling of the preauricular skin. Since this unusual mass lies beneath and in close proximity to the facial nerve, the conventional external approach to isolate the seventh cranial nerve is desirable and followed by intraoral excision of the mass. (Case I.)

### Case I. E.C.

45 year old male admitted to Hartford Hospital 1-18-61 with a 6 x 4 cm. mass beneath the right upper lateral pharyngeal mucosa of 6 months duration. No external parotid mass or cervical lymph node enlargement was noted. Remainder of workup including X-rays of base of skull and mandible were negative. A combined right external preauricular approach to expose and preserve the right facial nerve and intra-oral excision of the large tumor arising in the deep retromandibular lobe of the parotid was successful in removing this benign cellular mixed tumor. On his last followup visit 3-1-66 five years later, there was no evidence of recurrence.

If facial nerve weakness or paralysis, overlying skin ulceration, parotid pain or associated cervical lymph node enlargement are present with a history of rapid growth in the parotid mass, the diagnosis

of a primary malignant parotid tumor is justified. (Case II)

### Case II. S.C.

60 year old male admitted to Hartford Hospital 8-17-58 with a history of a mass in left parotid for 30 years which had recently increased in size and for the past six months had produced a left facial nerve paralysis. He was treated elsewhere as a left "Bell's palsy," without success for several months despite the presence of the hard parotid mass, progressive facial nerve paralysis and multiple enlarged firm cervical lymph nodes. He was admitted with the clinical diagnosis of carcinoma of left parotid. No evidence of systemic metastatic disease was noted on workup. Monoblock in continuity total resection of left parotid with facial nerve resection and radical neck dissection was carried out for an adenocarcinoma arising in a mixed tumor with lymphatic metastases. Two months after surgery, a course of post-operative radiation was given to the parotid bed. One year later, fascia lata slings to left face and left lateral canthoplasty restored facial symmetry. On his most recent followup visit, seven and one half years later, he is free of disease.

A slowly growing localized parotid mass without these accompanying signs may be considered a benign tumor especially since three of four salivary gland tumors are benign.

Diffuse swelling of the parotid is generally due to acute or chronic inflammation. While acute parotitis is rare in the adult, chronic, non-specific unilateral parotitis is more common and generally due to the recurrent sialolithiasis. When bilateral diffuse, symmetrical enlargement of the parotid is present, the diagnosis of chronic lymphocytic parotitis (Mikulicz' disease) suggests itself. Occasionally, either unilateral or bilateral hypertrophy of the masseter muscles may mimic a diffuse tumor of the parotid.

TABLE II  
HARTFORD HOSPITAL  
1936-1963  
PAROTID TUMORS

| CLASSIFICATION               | NUMBER | PER-<br>CENTAGE | AV. AGE | SEX RATIO |   |
|------------------------------|--------|-----------------|---------|-----------|---|
|                              |        |                 |         | F         | M |
| Benign                       |        |                 |         |           |   |
| Mixed tumor                  | 152    | 83%             | 51      | 2         | 1 |
| Adenolymphoma<br>(Warthin's) | 17     | 9%              | 59      | 1         | 4 |
| Hemangioma                   | 15     | 8%              | 5       | 1         | 1 |
|                              | 184    | 71%             |         |           |   |
| Malignant                    |        |                 |         |           |   |
| Cylindroma                   | 15     | 23%             | 47      | 3         | 1 |
| Muco-epidermoid              | 15     | 23%             | 40      | 1         | 3 |
| Adenocarcinoma               | 12     | 19%             | 55      | 1         | 1 |
| Squamous carcinoma           | 10     | 25%             | 57      | 1         | 3 |
| Undiff. carcinoma            | 5      | 10%             | 62      | 1         | 1 |
|                              | 63     | 29%             |         |           |   |

When unilateral progressive enlargement of the submaxillary or sublingual salivary gland is noted without local heat or tenderness, a primary tumor of these glands is to be considered with the expectation of a higher risk of malignancy than with parotid. Intermittent swelling, local pain and tenderness in the submaxillary and sublingual areas suggests inflammation with or without sialitis. Occasionally, a lymphoma containing node or nodes may be intimately adherent to the parotid or submaxillary glands simulating a primary tumor.

Fortunately, intra-oral mucosa minor salivary gland tumors are rare, but do have the characteristic appearance of a smooth, firm submucosal mass with intact overlying mucosa which slowly and inexorably increases until it outgrows its blood supply and undergoes central necrosis and ulceration. At this point, local pain and oral sepsis prompt a visit to the physician. Unfortunately, the majority of these tumors are malignant cylindromata which have a high potential for local recurrence.<sup>2</sup> Despite repeated excisions, ultimate death results due to extensive local recurrence, or occasionally, after long control of the primary, from bilateral diffuse hematogeneous pulmonary metastases. Case III.

**Case III. H.R.**

56 year old woman admitted to Hartford Hospital 2-21-50 with a smooth large non-ulcerated mass involving the entire base of tongue responsible for dysphagia and thickened speech. Biopsy revealed cylindroma. Chest X-ray was negative. An extensive resection of entire base of tongue was followed by a course of postoperative radiation. Despite this extensive surgery, patient was able to take a soft diet and speech was satisfactory, though thickened. Patient returned to her home in Oklahoma and had an uneventful seven years, following which dyspnea and unproductive cough prompted a return visit. Bilateral pulmonary metastases were demonstrated on chest X-ray and metastatic cylindroma noted on pleural biopsy at this time. No recurrence of the base of tongue primary was present. Despite X-ray and chemotherapy, the pulmonary disease was progressive and the patient expired in 1958.

One may encounter an unusual smooth mass in the hypopharynx, partly obstructing the critical air and food passages. While rare, these ectopic salivary gland tumors deserve adequate and prompt treatment. If benign, the prognosis is excellent. The case described is a benign mixed tumor arising on epiglottis, partly obstructing the airway. Case IV.

**Case IV. C.G.**

44 year old male laborer admitted to Hartford Hospital 7-29-63 with history of "lump in throat" and "huskiness" of voice. Indirect mirror examination revealed a smooth multilobular 4.0 cm. mass on ventricular surface of epiglottis. A median transhyoid approach permitted resection of this benign mixed tumor, ectopic salivary gland origin. Post-operative course uneventful. No recurrence noted on follow-up in January, 1966.

Large bulky cavernous hemangiomata involving the parotid and overlying skin may occur in the newborn infant. Rapid growth with extension toward orbit, mouth and neck make resection mandatory. Case V.

**Case V. J.B.**

Female infant seen in 1952 at eight weeks of age with a large cutaneous capillary and subcutaneous cavernous hemangioma of right parotid skin and gland. Despite X-ray therapy, the mass persisted and subsequently increased to a size of 5 x 3 x 3½ cm. At one year of age, this child had a resection of the right parotid gland and overlying skin. Facial nerve was identified and preserved and overlying involved skin deficit repaired using sliding malar flap. On last followup in 1966, fourteen years later, there was no recurrence.

It is well to remember that this excision is facilitated by exposure of the main trunk of the facial nerve at stylomastoid foramen, which in the newborn, is closer to the skin surface since the mastoid bone is flat and has not become pneumatized with air cells. This anatomical observation will aid the surgeon in his search of the facial nerve.<sup>1</sup>

**Technique**

Since the most common benign tumor of salivary gland, the mixed tumor, is pseudo-encapsulated, simple enucleation or limited excision will not result in complete removal. Additionally, multicentric foci of this neoplasm is not uncommon. Thus, a high recurrence rate may follow the limited operation.

On the other hand, a superficial lobectomy, removing the bulk of the superficial lobe lying lateral to the facial nerve will generally provide the best assurance against recurrence. In our group, (Table III) limited parotid excision was attended by 32 recurrences in 92 patients (35 per cent) in contrast to one recurrence noted in 62 consecutive cases (2 per cent) following superficial lobectomy.

When the superficial lobe is removed, immediate frozen section is made. If a benign report is rendered, the procedure is terminated. If frozen section indicates a malignant tumor of a low potential, the remainder of the deep lobe is removed, the

TABLE III  
HARTFORD HOSPITAL  
1936-1963  
INFLUENCE OF EXTENT OF SURGERY OF BENIGN  
PAROTID MIXED TUMORS

| OPERATION                                                     | NUMBER | RECURRENCE 5 YR.         |
|---------------------------------------------------------------|--------|--------------------------|
| Partial excision                                              | 90     | 32 (35%) *<br>**         |
| Subtotal excision                                             | 62     | 1 (1.6%)                 |
| * Capsule ruptured                                            | 12     | (5 recurrences followed) |
| ** Limited surgery<br>followed by X-ray,<br>radon seeds, etc. | 6      | (3 recurrences followed) |



facial nerve is preserved, a supra-hyoid neck dissection is carried out preserving the jugular vein and sternocleidomastoid muscle. If these nodes are involved, a total radical neck dissection, including the sternocleidomastoid muscle and jugular vein is carried out. Should the frozen section report indicate undifferentiated anaplastic tumor in the parotid, an in-continuity ipsilateral complete radical neck dissection is added to the total parotid resection. The facial nerve is sacrificed only if infiltrated by the tumor. X-ray therapy is generally given to the primary parotid bed in these undifferentiated neoplasms after wound healing is complete.

Increasingly, the recent graduates of surgical residencies are learning the technique of exposing and identifying the main trunk of the facial nerve as it exits from the stylomastoid foramen at the base of the skull, following it through the isthmus between the smaller deep retromandibular parotid lobe and the larger lateral superficial lobe with Stenson's duct, prior to removing the parotid tumor. Embryologically, the facial nerve and parotid gland arise from separate anlagen with a primary bifurcation of the nerve going over into the parotid gland which is extending posteriorly from the more anterior stomdeum.

An S shaped incision, virtually invisible when healed, is made in the preauricular skin sulcus, carried posteriorly behind the lobule of the ear and then swings anteriorly and inferiorly into the oblique hyoid crease. The skin flap containing the subcutaneous fat is then reflected forward off the parotid capsule. The lower pole of the parotid is elevated after the posterior facial vein and the greater auricular nerve are divided. Having identified the anterior border of the upper sternocleidomastoid muscle and posterior belly of the digastric muscle, the avascular plane between the external auditory canal cartilage and posterior parotid gland is entered. The main trunk of the facial nerve is found to exit from the stylomastoid foramen at a depth of 4-5 cm. from the skin surface at this level just above the mastoid attachment of the posterior belly of the digastric muscle. The nerve is followed through the parotid as it splits into two main divisions, the tempero-facial and cervical facial. With this critical step completed, the superficial lobe of the parotid is dissected from the nerve taking care to follow all branches and to preserve them. Bleeding points and Stenson's duct are controlled with ties of fine silk. A small 24-48 hour drain is placed in the lower angle of the wound which is closed in two layers with interrupted fine silk sutures.

Complications with this technique are few. Hemostasis is accurate. The facial nerve is visualized. No major salivary ducts are left incised and draining. Except for minimal and transient facial

| TABLE IV<br>HARTFORD HOSPITAL<br>1936-1963<br>RECURRENCE AND SURVIVAL RATES FOR PAROTID TUMORS |        |            |                |
|------------------------------------------------------------------------------------------------|--------|------------|----------------|
| CLASSIFICATION                                                                                 | NUMBER | RECURRENCE |                |
| Benign                                                                                         |        |            |                |
| Mixed tumor                                                                                    | 152    | 33 (22%)   |                |
| Adenolymphoma                                                                                  | 17     | 0 (0%)     |                |
| Hemangioma                                                                                     | 15     | 6 (40%)    |                |
| Malignant                                                                                      |        |            |                |
|                                                                                                |        |            | 5 YR. SURVIVAL |
| Cylindroma                                                                                     | 15     | 13 (86%)   | 8 (55%)        |
| Muco-epidermoid                                                                                | 15     | 6 (40%)    | 9 (60%)        |
| Adenocarcinoma                                                                                 | 12     | 9 (75%)    | 5 (40%)        |
| Squamous carcinoma                                                                             | 16     | 12 (75%)   | 4 (25%)        |
| Undiff. carcinoma                                                                              | 5      | 5 (100%)   | 1 (20%)        |
|                                                                                                | 63     | 45 (71%)   | 27 (42%)       |

nerve weakness, generally due to handling of the nerve during the dissection, there are no other significant complications. Frei's syndrone of gustatory sweating in the involved preauricular skin following mastication of food is found in about 10 per cent of patients who have had a subtotal parotid resection.

Results

75 per cent of the salivary gland tumors in our group were benign. Subtotal excision of the parotid gland with preservation of the nerve and complete resection of the submaxillary and sublingual glands for benign disease should be curative with a low rate of recurrence and morbidity.

The malignant tumors may range from low rate of recurrence and morbidity.

The malignant tumors may range from low grade cylindromas and muco-epidermoid tumors to the more aggressive adenocarcinomas. In this series there are 27 five year plus survivors out of 63 malignant parotid tumors for a total of 42 per cent five year survival. In this group of 63 patients there were 45 patients who presented recurrence after definitive surgical therapy (71 per cent), (Table IV). Total parotid resection with sacrifice of the facial nerve if it is directly involved, or preservation if uninvolved is the minimal operation recommended. In continuity radical neck dissections for enlarged metastatic nodes is mandatory. However, if the ipsilateral nodes are not enlarged and the primary tumor of low potential is present, one may defer neck dissection and observe the patient on subsequent followup visits. Supplementary X-ray therapy to the operative bed when the wound is healed is believed to be helpful, since adequate margins of resection for a malignant parotid tumor are difficult to achieve in the bony bed containing this salivary gland. Five year survival rates in the literature vary from 85 per cent five year survival

TABLE V  
HARTFORD HOSPITAL  
1936-1963

RESULTS OF TREATMENT OF MALIGNANT PAROTID TUMORS

| OPERATION         | NUMBER | TRACED | RECURRENCE | SURVIVAL |
|-------------------|--------|--------|------------|----------|
| Limited excision  | 2      | 2      | 0          | 2 (100%) |
| Subtotal excision | 18     | 15     | 3          | 13 (86%) |
| Total resection   | 2      | 2      | 0          | 2 (100%) |
| Total resection   | 9      | 6      | 1          | 5 (81%)  |
| Rad. neck diss.   |        |        |            |          |
| Radical surgery   | 7      | 5      | 3          | 3 (60%)  |
| & X-ray           |        |        |            |          |
| Limited surgery   | 14     | 13     | 3          | 4 (31%)  |
| & X-ray           |        |        |            |          |

with 35 per cent local recurrence for malignant tumors of moderate potential to 37 per cent five year survival with 73 per cent local recurrence for the tumors of a higher degree of malignancy.<sup>3</sup>

Our best results were achieved by total resection of the parotid in continuity with the ipsilateral neck nodes, followed by X-ray therapy to the parotid bed for neoplasms of low or moderate malignancy. Our poorest results were obtained in the highly aggressive squamous and undifferentiated carcinomas. See Tables IV and V.

#### Summary

The results of 290 primary tumors of salivary gland treated at the Hartford Hospital during the

25 year period of 1936-1963 are reviewed. Three fourths of this large group were benign. The lowest recurrence (2 per cent) and morbidity rate for this group was achieved by superficial lobectomy for parotid and total lobectomy for submaxillary, sublingual glands.

Malignant tumors of salivary glands have varying clinical courses depending upon their histology. The best results were obtained with total parotid resection in continuity with radical neck dissection, preserving the seventh nerve and followed by X-ray therapy to the parotid bed for tumors of low to moderate malignancy.

42 per cent of the entire group of malignant salivary gland tumors survived over five years in this series.

Selected case reports are presented to demonstrate diagnostic and therapeutic problems and their management.

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It is my temper and disposition to be careless of both the sayings and doings of the overproud and the overcritical. To the wise, however, and the honest, I wish to say this much: I have in no way whatever distorted either fact or experiment; I told the truth, the whole truth and nothing but the truth; and I have little fear but that they also, if they will make similar observations, will add their voices to mine. In the meanwhile I ask the pardon, and submit to the arguments, of better judges than myself for all errors of theory. Perhaps I may myself hereafter on many points change my mind of my own accord. As I have no lack of charity for the errors of others I have no love of obstinately persisting in my own.—*The Works of Thomas Sydenham, M.D.*, London. The Sydenham Society, 1847. Vol. 1, p. 28.



# The Management Of Patients With Malignant Lymphoma

Ronald C. DeConti, M.D. and Paul Calabresi, M.D.

## I. Introduction And Purpose

■ In the last two decades no group of patients with neoplastic disease has offered to the physician more opportunity for intellectual stimulation, scientific challenge and therapeutic reward than those designated by the term "Malignant Lymphoma." The protean manifestations of these disorders and their diverse complications have attracted the attention and concern of physicians with a wide variety of interests and training.

This article is intended to offer some general guidelines to the management of these disorders with emphasis on newer concepts in the use of radiotherapy and chemotherapeutic agents for the treatment of these complex diseases.

## II. Etiology, Classification And Differential Diagnosis

The etiology of the malignant lymphomas is unknown. While in the past all efforts to incriminate an infectious agent have failed, recent epidemiologic and viral evidence in the African lymphoma described by Burkitt,<sup>1,2</sup> may lend further support to the viral theory of oncogenesis.<sup>3</sup> Though grouped together by virtue of their similarities: (1) origin in lymph nodes, (2) neoplastic growth with widespread dissemination and ultimate death of the patient, and (3) similar responses to irradiation and chemotherapeutic agents, these malignant disorders have many dissimilarities in morphologic characteristics as well as mode and rate of progression.

An adequate biopsy specimen from an affected area is essential for the establishment of the diagnosis of malignant lymphoma. In general, it is preferable to avoid biopsy of the inguinal nodes, inasmuch as these nodes often are involved by chronic inflammatory processes unrelated to these disorders. Since many clinical and pathologic entities may mimic lymphomas, a clear-cut histologic distinction is necessary and a wide variety of processes

must be excluded. Some infectious diseases associated with lymphadenopathy—cat scratch fever, infectious mononucleosis, tuberculosis, syphilis, Q fever, toxoplasmosis and even rubella—may simulate lymphomas. Also confusing may be diseases of uncertain etiology—sarcoidosis, the histiocytoses, Wegener's granulomatosis, systemic mast cell disease, systemic lupus erythematosus, Sjorgren's syndrome, Mikulicz' syndrome and dermatopathic lymphadenopathy. Occasionally, a peculiar reaction to diphenylhydantoin<sup>4</sup> or related anticonvulsants may be difficult to distinguish from the lymphomas.

We have found useful a convenient classification of these disorders, modified after Rappaport<sup>5</sup> (see Table I). This classification has the virtues of describing both the proliferating cell type and the nodal architecture, avoids eponyms and may facilitate prognostic implications. Thus, a lymphoblastic lymphosarcoma would be classified as: malignant lymphoma lymphoblastic type, nodular pattern; or as malignant lymphoma, lymphoblastic type, diffuse pattern, depending on the architecture of the

TABLE I  
CLASSIFICATION OF THE MALIGNANT LYMPHOMAS

| DISEASE       | CELL TYPE                                        | NODAL ARCHITECTURE                                          |
|---------------|--------------------------------------------------|-------------------------------------------------------------|
| Hodgkin's     | Pleomorphic infiltrate with Reed-Sternberg cells | Nodular sclerosing<br>Paragranuloma<br>Granuloma<br>Sarcoma |
| Lymphosarcoma | Lymphocytic (well differentiated)                |                                                             |
|               | Lymphoblastic (poorly differentiated)            | Nodular ("follicular")                                      |
|               | Mixed (lymphocytic and reticulum cell)           |                                                             |
|               | Reticulum-cell                                   | Diffuse                                                     |

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Supported by Grants (T4 CA 5138-04, CA-05944, 5 MOI-FR-00038 and CA 8341-01) from the U.S. Public Health Service.

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node. Rappaport has emphasized the more favorable prognosis associated with a nodular or follicular pattern and many of these may be considered giant follicular lymphomas by other classifications.

While subclassification of the lymphomas may sometimes be difficult, special importance is attached to the diagnosis of Hodgkin's type and specimens should be examined thoroughly for the presence of the diagnostic Reed-Sternberg cell. This distinction may have important therapeutic consequences in patients with localized disease. A growing body of evidence suggests that, in contrast with lymphosarcoma, Hodgkin's disease may be unicentric in origin and usually spreads by contiguous extension, whereas the others appear to be either multicentric in origin or have a particularly rapid rate of dissemination with no predictable pattern of progression.

### III. Evaluation Of The Patient With Lymphoma

Although a lymphoma may involve almost any tissue or organ system and patients may present with such varied manifestations as tonsillar masses, gastrointestinal infiltrations or spinal cord compression, the most common initial evidence of lymphoma is peripheral lymphadenopathy, usually involving the cervical nodes. The physical examination should include a careful evaluation of the node-bearing areas and search for hepatosplenomegaly. The extent and degree of involvement should be carefully recorded in order to determine the rate of progression of the disease process. While patients with disseminated lymphosarcomas are often entirely asymptomatic for extended periods of time, the spread of Hodgkin's disease is often manifested by such constitutional symptoms as fever, night sweats, anorexia, weight loss and pruritus. Patients with occult retroperitoneal involvement by Hodgkin's disease may present with fever of unknown origin. This difference in the appearance of symptoms is frequently cited as evidence supporting an infectious etiology for Hodgkin's disease.

Important therapeutic considerations are derived from the fact that patients with lymphosarcoma frequently have multiple areas of involvement, while Hodgkin's disease often presents as a localized process, confined to one node or group of nodes. These observations, its natural history, and the evidence of its contiguous spread, together with the experience that adequate radiotherapy can often eradicate localized Hodgkin's disease, have led to the conviction that unlike lymphosarcomas, localized Hodgkin's disease is a potentially curable disorder.<sup>6</sup> In more extensive studies based upon the earlier experience of Gilchrist,<sup>7</sup> Peters and Middle-

TABLE II  
CLINICAL STAGING OF HODGKIN'S DISEASE

| STAGE | EXTENT OF DISEASE                                                                                                                                                         |
|-------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| I     | One group of lymph nodes involved.                                                                                                                                        |
| II    | Two or more groups of contiguous lymph nodes affected, but limited to one side of the diaphragm:<br>A. without constitutional symptoms<br>B. with constitutional symptoms |
| III   | Generalized disease above and below the diaphragm.                                                                                                                        |

miss<sup>8</sup> as well as Kaplan<sup>9,10</sup> have demonstrated improved survival using "radical dose" radiotherapy in patients with localized Hodgkin's disease. This evidence has emphasized the necessity to delineate and define the extent of Hodgkin's disease before treatment, in an effort to determine more precisely the clinical stage of disease. Table II defines the three clinical stages of the illness that have been widely adopted. In the past, variability in therapeutic response has been attributed to inaccurate staging since difficulty in assessing the presence of disease below the diaphragm may be responsible for including some patients with Stage III disease among those considered as Stage II. As might be expected, aggressive local therapy in the presence of widespread disease offers no advantage, and may even compromise future therapy by irrevocably damaging the bone marrow. In an endeavor to improve the accuracy of staging, a number of procedures have been developed in order to evaluate the retroperitoneal nodes when absence of inguinal nodes or splenomegaly makes this necessary. The most available procedure, intravenous pyelography, may be of value when ureteral displacement, distortion or obstruction are demonstrated. Unfortunately, this test is often erroneously negative when compared to the results of inferior vena-cavography or lymphangiography. Lee *et al*<sup>11</sup> have demonstrated that, in the presence of retroperitoneal lymphoma, intravenous pyelography was falsely negative in 70 per cent of the cases whereas lymphangiography demonstrated Stage III disease in approximately 50 per cent of patients initially classified as having Stage I and Hodgkin's disease. Of particular interest, 16 to 19 patients with Stage I lymphosarcoma and reticulum cell sarcoma were shown to have disseminated disease by this technique; a finding consistent with the hypothesis that these disorders have either a multicentric origin or a particularly rapid mode of spread.

These data, together with their prognostic and therapeutic implications, emphasize the necessity for thorough evaluation of every patient with Hodgkin's disease, utilizing lymphangiography when necessary. Though tedious and time-consuming, complications of this procedure have been in-



TABLE III

## STEPS IN THE EVALUATION OF PATIENTS WITH LYMPHOMA

1. Histologic confirmation of disease.
2. History with emphasis on development of constitutional symptoms.
3. Physical examination determining organ involvement and progression of disease.
4. X-ray examinations: Postero-anterior and lateral views of chest
  - Lymphangiography
  - Inferior venacavography
  - Intravenous pyelography
5. Hemopoiesis: Hemogram with platelet and reticulocyte counts
  - Bone marrow aspiration or biopsy
  - Pyrexal test
6. Stool examinations for occult blood.
7. Tests of liver function.
8. Tests of renal function: Urinalysis
  - Blood urea nitrogen or serum creatinine
9. Serum uric acid.
10. Alterations in serum proteins: Serum electrophoresis
11. Evidences of abnormal globulin production:
  - Coombs test
  - Serologic test for syphilis
  - Test for rheumatoid factor
  - Cryoglobulins
12. Skin test reactivity

frequent. In addition to allergic reactions, pulmonary and cerebral oil embolization have been reported<sup>12,13</sup> and the test is usually contraindicated in patients with significant pulmonary disease.

Recently, Herrera *et al*<sup>14</sup> have described the use of 75-Selenium labeled methionine to detect by external scanning the presence of occult lymphoma. At present, in cooperation with Dr. Richard Spencer, we are comparing the reliability of this innocuous procedure with that of lymphangiography. In previously unirradiated patients, initial results indicate good correlation between the two techniques and suggest a promising role for this test.

In addition to the fundamental considerations previously mentioned, Table III lists a number of specific studies that may be helpful in evaluating individual problems in patients with lymphoma.

Hematopoietic function may be assessed from peripheral blood studies and by aspiration or biopsy of the bone marrow. These studies may suggest a brisk hemolytic process, demonstrate bone marrow infiltration or herald transition to a leukosarcoma. Previous treatment with irradiation or drugs may have reduced cellularity and depleted bone marrow reserves and thereby limit future therapy. We are currently evaluating the granulocyte rise in response to an injection of purified *Salmonella* endotoxin (Pyrexal) for its value in pre-

dicting the degree of leukopenia produced by intravenous alkylating agents. Lack of response indicates diminished granulocyte reserve and warrants appropriate reduction in the dosage of these agents.

Occult blood in the stool may signal the presence of thrombocytopenia, bowel infiltration, or ulceration, possibly induced by corticosteroids.

Derangements in liver function may indicate hemolysis, obstruction, or infiltration. Jaundice is a sign of poor prognosis except in the rare instances when this is due to drug-induced or serum hepatitis. Levitan *et al*<sup>15</sup> have demonstrated that obstruction of the porta hepatis without intrinsic liver involvement is uncommon. The vinca alkaloids should be given with caution in jaundiced patients since impaired excretion by the liver may enhance their toxic potential.<sup>16</sup> Elevations in serum alkaline phosphatase are common in patients with extensive disease and the possibility of bone involvement should be considered.

Renal function tests may be helpful in diagnosing renal infiltration (most frequently encountered in reticulum cell sarcoma), ureteral obstruction, or radiation nephritis, and elevations of serum uric acid may call attention to the need for preventive measures to avoid nephrolithiasis and the precipitation of acute uric acid nephropathy. Increased catabolism of purines as a result of cellular destruction induced by rapidly effective oncolytic therapy with drugs or irradiation may result in hyperuricosuria and precipitation of uric acid crystals in the renal tubules with oliguria and, in severe cases, anuria.<sup>17,18</sup>

Many other studies may be undertaken in individual circumstances. The peculiar immunologic abnormalities and deficiencies of these patients are well recognized, if still unexplained. Two of these may have important clinical significance. Patients with lymphomas, particularly Hodgkin's disease, are often anergic when challenged with intradermal tests for delayed hypersensitivity.<sup>19</sup> A negative tuberculin test, therefore, is not helpful in excluding the diagnosis of tuberculosis. Patients with lymphosarcoma, unlike those with Hodgkin's disease, may have marked decreases in normal gamma globulin, a fact that may enhance their susceptibility to some bacterial infections, while evidence of abnormal antibody production may be manifested by various serological tests (see Table III).

#### IV. Selection Of Therapy

Once the diagnosis has been confirmed and the extent of disease defined, the physician should consider the advisability of treatment and the modality to be employed. The approach to therapy depends in part on the histologic type in question.

No treatment may be necessary or desirable for an asymptomatic patient with generalized lymphosarcoma, while recent evidence in Hodgkin's disease suggests that asymptomatic patients with a localized process should receive intensive radiotherapy in an attempt to eradicate the disease. There is little evidence to justify this therapy in apparently localized lymphocytic or reticulum cell sarcomas originating in lymph nodes; it is best to evaluate the rate of progression of the disease and withhold treatment until the biological aggressiveness of the disorder has been established. As in the treatment of other neoplastic conditions, three specific modalities of therapy may be considered: surgery, irradiation, and chemotherapy.

#### **SURGERY**

The major role of surgery in the management of lymphomas is to obtain an adequate surgical specimen for pathologic analysis. In the past, surgery has been advocated as primary treatment, particularly in localized Hodgkin's disease,<sup>20</sup> but most clinicians<sup>21-23</sup> now agree that survival of surgically treated patients is no better than that of irradiated patients and that local recurrences are frequent. Surgery may have a role in the treatment of those rare extranodal lymphomas primary in the stomach, intestine, lung, epidural space and parotid gland. In the later stages of the disease, surgery may provide valuable palliation for certain specific situations such as intractable pain, intestinal obstruction or extradural impingement on the spinal cord. In some patients, refractory hemolytic anemia may require splenectomy.

#### **RADIATION THERAPY**

The primary treatment of localized Hodgkin's disease (Stages I and II) is intensive radiotherapy designed to eradicate the process. This should be administered under the supervision of a trained radiotherapist. The optimum dose of radiation is as yet undetermined, though the experience is several investigators<sup>22</sup> including Scott<sup>24</sup> who has analyzed the linear dose relationships for the permanent arrest of Hodgkin's disease, indicates that at least 3,000-4,000 r in a 3 to 4 week period is necessary to prevent local recurrence. Influenced by the contiguous-spread hypothesis based on unicentric origin, Peters and Middlemiss<sup>8</sup> investigated the effect of prophylactic irradiation to clinically uninvolved proximal lymph node chains during primary treatment of Stage I and II Hodgkin's disease. Their data describe improvement in five year survival from 46 to 68 per cent, ten year survival from 31 to 53 per cent, and fifteen year survival from 26 to 43 per cent. This concept of



**FIGURE I**

This port film outlines the area irradiated in extended field radiotherapy. The left supraclavicular node area is the site of localized Hodgkin's disease.

prophylactic or extended field irradiation has been adopted by some, but not all, radiotherapists and has created sufficient interest to warrant organization of a national study to test this hypothesis. The introduction of supervoltage equipment offers the feasibility of delivering adequate dosages to larger areas in less time with fewer deleterious side-effects and thereby allows the possibility of conducting these trials with extended-field radiotherapy. The port film in Figure I illustrates the field of irradiation used in this program.

While the intent of radiation therapy in localized Hodgkin's disease is curative, the role of therapy in Stage III Hodgkin's disease and the other lymphomas is supportive and palliative. In these situations radiotherapy is designed to reduce or eradicate particularly troublesome or symptomatic localized areas of involvement. Lymphomatous infiltration may involve almost any tissue or organ in the body. Some common clinical problems, which are often responsive to treatment with irradiation, are listed in Table IV. Lymphatic obstruction may foster the development of lymphedema and the accumulation of pleural fluid. Local tumor masses resulting in obstruction of the airway, the ureters, or the gastrointestinal tract should be treated without delay. Compression of the superior vena cava or spinal cord constitute emergency situations requiring immediate attention. In these critical areas where precarious limitation of space makes even a minimal swelling a dangerous



TABLE IV  
USES OF RADIOTHERAPY IN PATIENTS WITH LYMPHOMA

| AIM                      | CLINICAL SITUATION                                                                                                                                                                                                                                       |
|--------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Eradication of disease   | Hodgkins disease, Stages I and II<br>Reticulum cell sarcoma, primary in bone.<br>Extranodal lymphosarcoma, localized (pharynx, tonsil)                                                                                                                   |
| Preservation of function | Pleural effusion due to mediastinal disease<br>Lymphedema of the extremities<br>Air-way obstruction<br>Ureteral obstruction<br>Intestinal obstruction<br>Superior vena caval syndrome<br>Spinal cord compression<br>Neural infiltration<br>Hypersplenism |
| Relief of pain           | Node masses<br>Bone infiltration                                                                                                                                                                                                                         |

risk, special measures must be taken to avoid radiation edema. These usually consist of concomitant administration of corticosteroids (prednisone 40 mg/day) and conservative initial doses of X-ray, such as 25 to 50 r gradually increased by small daily increments; where cord compression is rapidly advancing, irradiation should follow neurosurgical intervention. In general, the indications for radiotherapy must take into consideration the gain of local therapy with respect to the influence of irradiation on the overall status of the patient's present health and ultimate survival. In some situations the advantages of radiotherapy may be less certain and, if the disease process is generalized, chemotherapy may be preferred as initial treatment, reserving radio-therapy for unresponsive localized lesions.

CHEMOTHERAPY

While unequivocal statistical evidence that chemotherapeutic agents have prolonged the overall survival of patients with lymphoma, is not yet available, there is ample clinical experience to document the ability of these agents to improve greatly the quality and duration of survival in individual patients. Usually, therapy is initiated after assessment of the patient has revealed generalized progressive disease, with or without constitutional symptoms. The rapidity of progression and the clinical severity of the disease will often influence the choice of agent to be employed. Perhaps it should be emphasized that lack of constitutional symptoms, in the face of advancing disease, should not deter the physician from initiating therapy. Much better clinical responses are to be expected by anticipating the need for palliation rather than by withholding treatment until emaciation or severe debilitation has depleted the natural resis-

tance of the host. Inasmuch as many chemotherapeutic agents impair wound healing and interfere with the body's resistance to infection, we do not advocate the use of these drugs in the immediate post-operative period or in the presence of infection.

V. Effective Chemotherapeutic Agents In The Control Of Lymphomas

Antineoplastic agents may be divided into five classes:<sup>25</sup> antimetabolites, alkylating agents, natural products, hormones and a miscellaneous group. While leukemia, mycosis fungoides, psoriasis, and selected non-lymphoid tumors have been responsive to various antimetabolites, these agents have been of little clinical value in the treatment of lymphomas and, except for investigational purposes, are not currently used in the management of these disorders.

ALKYLATING AGENTS

The first clinical trials of the parent compound of this group of agents, mechlorethamine hydrochloride (HN2, Mustargen®) were conducted at Yale in patients with malignant lymphoma by Gilman, Goodman and Dougherty in collaboration with G. E. Lindskog in 1942. During the next decade the dosage schedules and clinical spectra of activity were explored and, despite studies with many derivatives, this compound still serves as the standard of reference and unequivocal evidence of superior antineoplastic effects of new agents in this class has not been demonstrated.

Of many alkylating agents synthesized, only three will be considered: mechlorethamine hydrochloride (HN2, Mustargen®), cyclophosphamide (Cytosan®), and chlorambucil (Leukeran®). These have been selected because of their demonstrated clinical effectiveness and because each offers several selective features that may be of advantage in various clinical situations.

HN2 has the advantage of rapid antineoplastic action, sometimes beginning within 1 or 2 days after administration but, because of its unusual reactivity, the solution must be freshly prepared and administered through a rapid intravenous infusion. The total dose (0.2 to 0.4 mg/kg) should be given as a single injection, since there is no therapeutic advantage to dividing the dose and the patient is spared prolongation of the emetic effects. Because of its vesicant action, extravasation of the drug will result in painful thrombophlebitis, tissue necrosis and possible sloughing with residual contractures. Prompt infiltration of the area with sodium thiosulphate may minimize this complication. Cyclophosphamide, a cyclic phosphamide ester, is relatively inert *in vitro* and lacks the local vesicant

effect of HN2 when given intravenously. When administered in large intravenous doses (30 to 40 mg/kg), it is comparable to HN2 in speed of action. Both drugs produce nausea and vomiting, though the reactions to HN2 are often more severe and the patients should be premedicated with antiemetics and sedatives. While cyclophosphamide is somewhat better tolerated, it may produce two side effects not noted with HN2: alopecia and, less frequently, sterile hemorrhagic cystitis.<sup>26</sup> Alopecia is reversible even without discontinuation of therapy while the cystitis, which is caused by products of hydrolysis, subsides after cessation of drug.

Cyclophosphamide and chlorambucil have the advantage of oral administration. When given by

mouth, cyclophosphamide is intermediate in action, usually requiring 1 to 3 weeks before antineoplastic effects are noted, while chlorambucil has a comparatively slower effect, often requiring 2 to 6 weeks of therapy to achieve therapeutic response. At usual dosages (6 to 12 mg/day), chlorambucil is without symptomatic effects, while in the dose range of 200 to 300 mg/day cyclophosphamide may produce some anorexia, nausea and even vomiting.

The limiting toxicity of these agents is bone marrow suppression with leukopenia and thrombocytopenia, which may allow the development of infectious or hemorrhagic complications. Evaluation of the peripheral blood, the bone marrow, and the granulocyte response to endotoxin stimulation

TABLE V  
SPECIFIC AGENTS IN THE CHEMOTHERAPY OF LYMPHOMA

| CLASS             | AGENT                                              | BRAND NAME | USUAL DOSAGE                                  | ONSET OF CLINICAL RESPONSE | UNTOWARD EFFECTS                                                                                                                                                                                                                                                                 |
|-------------------|----------------------------------------------------|------------|-----------------------------------------------|----------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Alkylating agents | Mechlorethamine HCl (HN2)                          | Mustargen  | Single dose<br>0.2-0.4 mg/kg<br>Intravenously | 1-21 days                  | Nausea and vomiting.<br>Vesicant action with phlebitis and tissue necrosis.<br>Leukopenia and thrombocytopenia.                                                                                                                                                                  |
|                   | Cyclophosphamide                                   | Cytosan    | Single dose<br>20-40 mg/kg<br>Intravenously   | 1-21 days                  | Less nausea and vomiting than HN2.<br>No local irritative effects.<br>Leukopenia, less thrombocytopenia than HN2.<br>Alopecia.                                                                                                                                                   |
|                   |                                                    |            | 2-5 mg/kg/day<br>Orally                       | 1-3 weeks                  | Hemorrhagic cystitis.                                                                                                                                                                                                                                                            |
| Natural products  | Chlorambucil                                       | Leukeran   | 0.1-0.2 mg/kg/day<br>Orally                   | 2-6 weeks                  | Gradual leukopenia and thrombocytopenia.                                                                                                                                                                                                                                         |
|                   | Vinblastine                                        | Velban     | 0.1-0.4 mg/kg<br>weekly<br>Intravenously      | 1-3 weeks                  | Leukopenia.<br>Temporary mental depression, mild paresthesias and occasional loss of deep tendon reflexes.                                                                                                                                                                       |
|                   | Vincristine                                        | Oncovin    | 0.01-0.04 mg/kg<br>weekly<br>Intravenously    | 1-3 weeks                  | Local irritation, inflammation and phlebitis.<br>Paresthesias, loss of deep tendon reflexes, neuritic pain, foot-drop and inability to walk, hoarseness, ptosis and double vision, severe constipation and colicky abdominal pain.<br>Alopecia.<br>Little effect on bone marrow. |
| Glucocorticoids   | Prednisone                                         | Meticorten | 10-80 mg/day<br>Orally                        | 1-7 weeks                  | Fluid retention, hypertension, diabetes, mental aberrations, peptic ulceration and increased susceptibility to infection.                                                                                                                                                        |
| Miscellaneous     | N-isopropyl-a-(2-methyl hydrazine)-p-toluamide HCl | Natulan    | 1-4 mg/kg/day<br>Orally                       | 1-3 weeks                  | Anorexia, nausea and vomiting.<br>Leukopenia and thrombocytopenia.<br>Mental aberrations.                                                                                                                                                                                        |



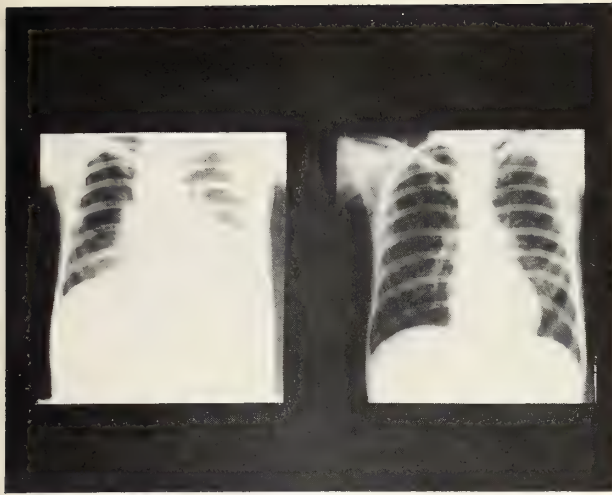


FIGURE II

Marked reduction in mediastinal involvement three weeks after initiation of vinblastine therapy in this young man with Hodgkin's disease.

(Pyrexal test) may be useful guides for planning the dosage of the drugs. The nadir of depression of the leukocyte and platelet count usually occurs 7 to 14 days after a single intravenous dose of either HN2 or cyclophosphamide. Clinical evidence suggests that at comparable levels of leukopenia, cyclophosphamide produces considerably less thrombocytopenia than HN2. This selective sparing of the megakaryocytes may offer therapeutic advantage in situations where platelet counts are already depressed by marrow infiltration, irradiation or previous drug therapy.

In the past, repeated courses of HN2 have been given at 4 to 8 week intervals or only after relapse; the results of the Western Cancer Chemotherapy Group, however, clearly demonstrate the superiority of maintenance oral therapy in preventing relapse.<sup>27</sup> In this study administration of chlorambucil after initial remission with HN2, prolonged the mean duration of this response to more than 36 weeks, as compared to average remissions of 11 weeks in patients receiving HN2 alone. Accordingly, after initial intravenous therapy with HN2 or cyclophosphamide, either chlorambucil or cyclophosphamide should be administered 2 to 3 weeks later, when serial leukocyte counts indicate recovery from leukopenia. In general, reduced dosages of chlorambucil (4 to 6 mg/day) or cyclophosphamide (50 to 150 mg/day) should be initiated and gradually increased over the next several weeks as recovery of the marrow continues. Therapy should be monitored with weekly blood counts and maintenance continued until either leukopenia or relapse occurs. Before the drug is considered a failure, it should be given in dosages that produce

moderate leukopenia without achieving a satisfactory therapeutic response.

The overall effectiveness of this group of agents in the lymphomas has been well studied. The most favorable response rates occur in Hodgkin's disease (40 per cent to 80 per cent). The lymphocytic lymphosarcomas respond somewhat less often and the responses in reticulum cell sarcoma, though sometimes dramatic, tend to be of short duration and difficult to maintain. Despite these limitations, this group of agents usually constitute our first choice for chemotherapy of these disorders. The vinca alkaloids closely parallel the alkylating agents in therapeutic efficacy and may even be preferable in certain situations.

#### NATURAL PRODUCTS

Two derivatives of the periwinkle plant, *Vinca Rosea Linn*, have been investigated clinically during the past six years and have demonstrated remarkable anti-neoplastic effects in the lymphomas. Vinblastine (Velban®), has been very successful in the treatment of Hodgkin's disease and may be used as the initial chemotherapeutic agent in this disorder.<sup>28</sup> Vincristine (Oncovin®) has been less impressive in controlling Hodgkin's disease, but has yielded good results in lymphocytic lymphosarcoma and some activity against reticulum cell sarcoma. Other natural products such as the colchicine derivative demecolcin (colcemid®), or the antibiotics actinomycin D (Dactinomycin®) and streptonigrin have been reported to be of value in the treatment of lymphomas,<sup>29-31</sup> but the incidence and quality of response, as well as the toxicity of these agents, have limited their general use.

Despite considerable studies,<sup>16</sup> the mechanism of action of the vinca alkaloids is not known. It is clear, however, that the slight structural difference between vinblastine and vincristine—replacement of formyl group by a methyl group—produces profound differences in the biologic activity of the compounds. While both are given intravenously and may produce local inflammatory changes, the dosages, clinical toxicity and therapeutic responses differ considerably.

Vinblastine is given weekly in dosages increasing from 0.1 to 0.4 mg/kg of body weight. Bone marrow suppression, manifested chiefly by leukopenia, is generally the dose-limiting factor. The nadir of leukopenia usually occurs within 4 to 10 days with recovery ensuing thereafter. Therapy is usually begun with 0.1 mg/kg and is increased by weekly increments until the occurrence of either moderate leukopenia or beneficial response. Persistent leukopenia may limit dosage to intervals of 14 days but continued therapy is necessary to avoid relapse,



FIGURE III

Marked reduction in supraclavicular adenopathy one month after initiation of vinblastine therapy for generalized Hodgkin's disease. This remission was continued for twenty-seven months utilizing maintenance dosages of vinblastine.

which usually occurs within 3 weeks of the last injection. Leukopenia is the major factor to be considered in regulating the dosage; neurologic complaints such as temporary mental depression, paresthesias, loss of deep-tendon reflexes and autonomic dysfunction may occur, but are generally mild. Vincristine is also given intravenously, but in weekly dosages one-tenth those of vinblastine. These doses (0.01-0.04 mg/kg) rarely result in leukopenia but may produce profound paresthesias, loss of reflexes, neuritic pain, and muscle weakness with footdrop, inability to walk, hoarseness, ptosis and double vision. These neurologic complications are the dose-limiting features and the more severe manifestations can be avoided either by suspending therapy or reducing dosage with development of the earliest symptoms, usually tingling and numbness of the finger tips. Vincristine may produce severe constipation and may cause abdominal pain simulating intestinal obstruction; both can be prevented by a prophylactic program of mild laxatives and hydrophilic agents. Alopecia may occur in 20 per cent of patients treated with vincristine but is an uncommon effect of vinblastine.

In Hodgkin's disease, judicious administration of vinblastine every 7 to 14 days produces objective remissions comparable to those obtained with the alkylating agents. With regular injections of vinblastine it is possible to maintain long-term remis-

sions with minimal toxicity. This quality and duration of response is achieved much less often in the other lymphomas. Studies are currently underway to investigate the possible therapeutic advantages of combination therapy utilizing low dosages of vinblastine and chlorambucil.<sup>32, 33</sup>

While response rates with vincristine may be relatively high in patients with lymphosarcoma, the duration of response does not compare with those seen in Hodgkin's disease treated with vinblastine. In our experience 67 per cent of patients with lymphosarcoma responded, but the mean duration of response was only 3 months.<sup>34</sup> The brevity of response and the low therapeutic index has limited the usefulness of vincristine to special situations where it is of unique advantage. In conventional dosages, vincristine has minimal myelosuppressive effects and is of great value when marrow infiltration or previous therapy with drugs and irradiation preclude the use of alkylating agents or vinblastine. Indeed, we have seen improvement in marrow function during therapy with vincristine, since the action upon the neoplastic infiltration of the marrow is not accompanied by a similar deleterious effect upon the normal hemotopoietic elements.

A most important aspect of therapy in the management of patients with lymphoma is the lack of cross resistance between classes of drugs. A patient



whose disease is no longer controlled by alkylating agents may well obtain a complete remission after treatment with vinblastine. Similarly, patients unresponsive to vinblastine may respond to alkylating agents. While responses to different alkylating agents are usually similar, patients resistant to vinblastine may still respond to vincristine. This lack of cross resistance and the differing toxicities of the vinca alkaloids allows the sequential use of these drugs and increases the likelihood of inducing or prolonging remissions with this class of agents.

**HORMONES**

The adrenocorticosteroids are temporarily successful in suppressing symptoms of fatigue, lethargy, weakness, anorexia and fever in a great majority of patients with lymphomas and, as such, constitute a valuable adjunct in the management of these individuals. Some patients, particularly those with lymphosarcoma, may experience striking regression of adenopathy when prednisone is used in doses ranging from 10 to 80 mg/day.<sup>35</sup> This improvement is presumably the result of the lympholytic effects of corticosteroids and their ability to suppress mitoses in lymphocytes.<sup>36</sup> These beneficial effects, however, are usually short-lived and the patient risks a number of possible complications including infection, peptic ulceration, hypertension and the cushingoid state. Usually, corticosteroids merely provide symptomatic palliation and, unfortunately, these agents are often abused by being employed early in the course of the illness in place of other drugs that might induce prolonged objective remissions with fewer hazards. We are inclined to reserve this form of therapy for patients with far-advanced disease, unresponsive to other modes of treatment. More commonly, we have used moderate-to-high dosages (prednisone 40 to 80 mg/day) in an effort to terminate an episode of frank hemolytic anemia, to prevent or alleviate the hemorrhagic complications of thrombocytopenia, or to obtain temporary but rapid control of the disease process in severely ill patients. Corticosteroids are also effective for the prevention of edema induced by radiation in the treatment of superior vena caval syndromes, spinal cord compression or intracranial involvement. Relatively low doses of prednisone (15 to 30 mg/day) are useful for supporting a patient symptomatically until an oncolytic agent results in remission or until the leukopenia from previous therapy has remitted enough to allow institution of another myelosuppressive drug.

**MISCELLANEOUS**

The most promising investigational agent to be developed since the advent of the vinca alkaloids

appears to be the methylhydrazine derivative (N-isopropyl- $\alpha$ -(2-methylhydrazine)-p-tolamide hydrochloride, Natulan®). Though its mechanism of action is unknown, early studies<sup>37,38</sup> have demonstrated its effectiveness in Hodgkin's disease, but up to date have not been particularly encouraging in other lymphomas. Our own investigations with this drug have demonstrated substantial clinical benefits in 8 of 13 patients with far-advanced Hodgkin's disease. The drug is administered orally, may produce nausea and vomiting during the first few days of therapy, and usually requires 1 to 3 weeks to induce remission; leukopenia and thrombocytopenia are the major factors limiting dosage. The data do not indicate cross resistance with alkylating agents or the vinca alkaloids and suggest that this drug may be of definite advantage in patients no longer responsive to these agents. Further studies will be necessary to determine the long-term role of this class of agents in our therapeutic armamentarium.

**VI. Special Problems And Complications In Management**

Episodes of pyrexia, chills and excessive perspiration are common accompaniments of Hodgkin's disease in relapse and generally respond promptly to effective chemotherapy. While awaiting such response, these symptoms are usually controlled by the regular administration of salicylates; in refractory cases, indomethacin or aminopyrine may be used to advantage. The immunologic deficiencies of these patients, however, as well as their peculiar susceptibility to certain infections, require careful evaluation of all febrile episodes.

Bacterial infections are common in patients with lymphosarcomas, particularly in association with hypogammaglobulinemia.<sup>39</sup> These range from staphylococcal or pneumococcal pneumonias to fulminant septicemias due to various gram-negative organisms. In Hodgkin's disease, host resistance to the usual bacterial infection is maintained until late in the course of the disease. Because these patients are unduly susceptible to tuberculosis, however, smears and cultures for acid-fast organisms should be performed, especially when fever is associated with stiff neck, headache, pulmonary infiltration or pleural effusion. Because of the deleterious activation of tuberculosis which may occur as a result of corticosteroid therapy, it has become our custom to begin prophylactic isoniazid when prednisone therapy in dosages greater than 30 mg/day is administered.

Of the mycotic infections, moniliasis and cryptococcosis occur most frequently. Localized moniliasis, involving the oral pharynx or the vagina, is

generally readily apparent and involvement of the esophagus should be suspected when dysphagia accompanies the oral lesions; local treatment with mycostatin is generally rapidly effective in controlling the infection. Systemic moniliasis is much less common and requires intravenous therapy with amphotericin B. Cryptococcosis usually presents as a subacute meningitis and objective evidence of cerebral involvement may be minimal; careful examination of the spinal fluid using india-ink will frequently demonstrate the organism.

A number of viral infections are of special importance. Herpes zoster is the single most frequently documented viral infection and the most common neurologic complication of lymphomas.<sup>40</sup> Nerve-root pain may produce considerable clinical confusion until the eruption of the rash identifies the cause. Fortunately, most episodes respond to symptomatic treatment alone. Generalized vaccinia is a rare but potentially lethal infection in patients with lymphosarcoma and vaccination of patients with these disorders should be avoided. Recent investigations have demonstrated the presence of cytomegalovirus in patients with lymphomas.<sup>41</sup> The role of this organism in the pathogenesis of clinical infection remains to be determined and future work will undoubtedly reveal still other occult viral infections.

Patients with lymphomas are subject to a variety of metabolic disorders. While the development of secondary gout is frequently recognized, relatively less attention has been devoted to the renal complications related to hyperuricemia and hyperuricosuria. Hyperuricosuria may often be present even without hyperuricemia<sup>42</sup> and this probably explains the increased incidence of renal lithiasis in these patients.<sup>43</sup> Of greater hazard to the patient is the sudden increase in concentration of uric acid in the renal tubule as a consequence of rapid and effective oncolytic therapy, which may precipitate

TABLE VI  
SOME INFECTIOUS COMPLICATIONS OF LYMPHOMA

|            |                                                                                                         |
|------------|---------------------------------------------------------------------------------------------------------|
| Bacterial: | Staphylococcal infections<br>Pneumococcal pneumonia<br>Gram-negative sepsis<br>Tuberculosis             |
| Fungal:    | Localized moniliasis<br>oral<br>esophageal<br>vaginal<br>Systemic moniliasis<br>Cryptococcal meningitis |
| Viral:     | Herpes zoster<br>Progressive vaccinia<br>Cytomegalovirus                                                |

TABLE VII  
POSSIBLE METABOLIC COMPLICATIONS OF LYMPHOMA

1. Renal lithiasis due to chronic hyperuricemia.
2. Acute uric acid nephropathy due to oncolytic therapy.
3. Azotemia due to dehydration, infiltration, obstruction or amyloid disease.
4. Metabolic acidosis due to renal infiltration.
5. Respiratory acidosis due to lymphangitic spread of lymphoma.
6. Lactic acidosis of unknown cause.
7. Malabsorption due to small bowel involvement.
8. Hypercalcemia.
9. Alcohol-induced pain.

acute uric acid nephropathy with oliguria and even anuria. In addition to the established use of hydration and alkalinization of the urine, our recent experience with allopurinol demonstrates that this inhibitor of xanthine oxidase can effectively prevent or abort this potentially dangerous complication.<sup>44</sup> By blocking the formation of uric acid, the oxypurines, xanthine and hypoxanthine, are excreted without exceeding their solubility products. Dramatic falls in serum uric acid and in the excretion of uric acid are usually obtained in 24 to 48 hours. The use of allopurinol in conjunction with antineoplastic therapy introduces a new measure of safety to the management of these disorders.

Azotemia may also be the direct result of obstruction or infiltration of the renal parenchyma and, in later stages, can result in metabolic acidosis. In addition to renal causes of acidosis, lactic acidosis of unknown etiology has been reported<sup>45</sup> and even respiratory acidosis can result from pulmonary lymphangitic involvement by lymphoma. Vitamin deficiency and malabsorption may occasionally develop as a consequence of extensive small bowel involvement<sup>46</sup> and appropriate replacement therapy may be beneficial. Hypercalcemia may be an unsuspected cause of anorexia, nausea, and vomiting, even in patients without clinical or roentgenographic evidence of skeletal lesions.<sup>47</sup> Fortunately, this complication is usually readily reversed by corticosteroid therapy. A fascinating but totally unexplained phenomenon in some patients with lymphomas, particularly Hodgkin's disease, is the development of pain in areas of active disease within a few minutes after the ingestion of even small quantities of alcohol.<sup>48</sup>

VII. Accomplishments

The experience of the last two decades has brought about a gradual transition in our attitudes and expectations in the treatment of the malignant lymphomas. While our understanding of the etiology of neoplastic cellular proliferation leaves much



to be desired, we have achieved a great deal in the management of these complex disorders and the physician need no longer disconsolately admit helplessness. Recent advances in techniques utilizing high-dose irradiation therapy in Stage I and II Hodgkin's disease have improved survival and fostered concepts of long-term arrest—and even “cure”—of what was once considered to be a rapidly and irrevocably fatal disorder. Refinements in our usage of the alkylating agents and the development of new classes of antineoplastic drugs, offer the physician a greater opportunity to palliate effectively and to rehabilitate completely a growing number of patients with malignant lymphomas. Our increasing ability to maintain remissions, to reduce suffering and morbidity, and to restore many of these patients to happy and productive lives, warrants measured optimism and even greater expectations for the future.

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The interests of society are discovered by usage and moral law reflects the residual experience of man. "Knowledge comes and wisdom lingers." As we have seen with the railroad, society insists on a control of whatever new invention radically affects the lives of all of us—and even propriety rights provide no immunity to society's insistent demands. So in the last analysis any new tool, any new machine, any new institution, first passes through a stage of virile independence and self-reliance but in the end is restrained by the relentless insistence of those whose lives are affected by it and reflects where it does not depend upon public policy. Medical research is, I think no exception, for it is too influential to remain entirely unregulated.—Alan Gregg: *The Furtherance of Medical Research*, New Haven. Yale University Press, 1941, p. 20.





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## Contraindications

Edema, danger of cardiac decompensation; history or symptoms of peptic ulcer; renal, hepatic or cardiac damage; history of drug allergy; history of blood dyscrasia. The drug should not be given when the patient is senile, or when other potent drugs are given concurrently. Large doses are contraindicated in patients with glaucoma.

## Precautions

Obtain a detailed history and a complete physical and laboratory examination, includ-

ing a blood count. The patient should be closely supervised and should be warned to report immediately fever, sore throat, or mouth lesions (symptoms of blood dyscrasia); sudden weight gain (water retention); skin reactions; black or tarry stools. Make regular blood counts. Use greater care in the elderly.

## Warning

If coumarin-type anticoagulants are given simultaneously, watch for excessive increase in prothrombin time. Pyrazole compounds may potentiate the pharmacologic action of sulfonyleurea, sulfonamide-type agents and insulin. Carefully observe patients receiving such therapy.

## Adverse Reactions

The most common are nausea, edema and drug rash. Hemodilution may cause moderate fall in red cell count. The drug may reactivate a latent peptic ulcer. Infrequently, agranulocytosis, generalized allergic reaction, stomatitis, salivary gland enlargement, vertigo and languor may occur. Leukemia and leukemoid reactions have been reported but cannot definitely be attributed to the drug. Thrombocytopenic purpura and aplastic anemia may occur. Confusional states, agitation, headache, blurred vision, optic neuritis and transient hearing loss

have been reported, as have hepatitis, jaundice, and several cases of anuria and hematuria. With long-term use, reversible thyroid hyperplasia may occur infrequently.

## Dosage

The initial daily dosage in adults is 300-600 mg. daily in divided doses. In most instances, 400 mg. daily is sufficient. When improvement occurs, dosage should be decreased to the minimum effective level: this should not exceed 400 mg. daily, and is often achieved with only 100-200 mg. daily.

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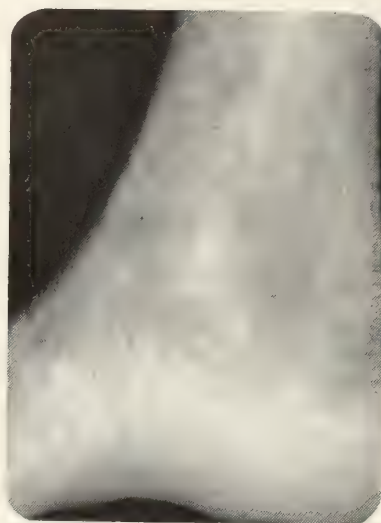
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*Precautions and Side Effects:* Do not use in the eyes or in the ear (if drum is perforated). A few individuals react unfavorably under certain conditions. If side effects are encountered, the drug should be discontinued and appropriate

measures taken. Use on infected areas should be attended with caution and observation, bearing in mind the potential spreading of infection and the advisability of discontinuing therapy and/or initiating antibacterial measures. Generalized dermatological conditions may require systemic corticosteroid therapy. Steroid therapy, although responsible for remissions of dermatoses, especially of allergic origin cannot be expected to prevent recurrence. The use over extensive body areas, with or without occlusive nonpermeable dressings, may result in systemic absorption. Appropriate precautions should be taken. When occlusive nonpermeable dressings are used, miliaria, folliculitis and pyoderma will sometimes develop. Localized atrophy and striae have been reported with the use of steroids by the occlusive technique. When occlusive nonpermeable dressings are used, the physician should be aware of the hazards of suffocation and flammability. The safety of use on pregnant patients has not been firmly established. Thus, do not use in large amounts or for long periods of time on pregnant patients.

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## THE PRESIDENT'S PAGE

**T**ITLE XVIII of P.L. 89-97—the so-called Medicare Law—became effective as of July 1. On that date, 19 million Americans age 65 or over became entitled to certain *hospital benefits* (Part A), not only those who are eligible to receive Social Security cash benefits but also a considerable number who are not. This part of the Medicare program will be financed by a combination of payroll taxes and general funds.

Approximately ninety per cent of the same group have also enrolled for Part B, with the enrollee and the government contributing equally to the monthly “premium” of \$6. Part B proposes to furnish certain *medical benefits*, including payment for physicians’ services, and carries with it a \$50 annual deductible and a 20 per cent co-insurance obligation which must be met by the patient.

In addition, Title XIX of the same P.L. 89-97 was implemented in Connecticut on the first of this month, offering a comprehensive tax-supported medical care program to many thousands of persons in indigent and medically-indigent categories who may be of practically any age. Again, the coverage provides for payment for physicians’ services—in the office, in the home, and in the hospital.

Quite apart from perfectly natural professional concern as to how the rules and regulations of these revolutionary programs may affect the quality of medical care rendered by the practitioner—the maintainance of which is his responsibility—a good deal of emphasis has necessarily had to be placed on trying to establish a fair and equitable basis for compensating him for his services.

Government, at all levels, has elected to utilize established insurance and prepayment agencies as “fiscal intermediaries” or “carriers” for various parts of Title XVIII and Title XIX. In principle, at least, this appears to have been a wise move, since most doctors have had considerable previous experience in dealing with voluntary third parties. On the other hand, Medicare (in particular) has largely put the voluntary plans out of business in the area of providing basic health coverage for the elderly. Being forced to cancel supposedly non-cancellable policies which they had made available to so many over-65’s in the past, they are now limited in the voluntary sector to offering “supplementary” coverage to help fill the loopholes in Parts A and B. As intermediaries for Medicare, of course, they are agents of the Federal government and are required to comply with all regulations laid down by the Social Security Administration.

The Connecticut General Life Insurance Company has been awarded the contract to administer Part B in this state, and the company has gone to considerable pains to inform all practitioners of how they expect to operate the program. The basis for reimbursement, they say, will be the individual physician’s “usual” fee in relation to “customary” or “prevailing” charges in his area of practice for similar services of similar competence. However, the word “reasonable” has been insisted on by the government as a modifying adjective to the foregoing definitions, and it remains to be seen to what extent this modification will exert its influence on Connecticut General’s intended policy of paying usual and customary charges (actually, 80 per cent of same) for Medicare beneficiaries. Certainly no doctor is in favor of “unreasonable” payments, but it seems unlikely that very many could be even partially deluded for very long by what might amount to a play on words.

On April 26, the House of Delegates of the Connecticut State Medical Society took a firm and forthright stand to the effect that, in all instances in which a third party, private or public, contracts with people to pay all or part of their doctor bills, the basis on which the agency fulfills its part of the contract should be the physician’s usual and customary charges, *as determined at local level*. Should questions arise in this regard, such questions should be referred for opinion to a review committee of the county medical association having jurisdiction in the physician’s area of practice.

Under Medicare B, the advantages of direct billing of the patient vs. taking assignment of benefits from the carrier should be given most careful consideration by each of us. In my opinion, it is far wiser to come to a mutually satisfactory agreement with our patients on what is a “reasonable” charge, than it is to leave this determination to any third party—however well-intentioned.

ORVAN W. HESS, M.D.

# FROM THE GENERAL MANAGER'S OFFICE

WILLIAM R. RICHARDS, M.D., *General Manager*

Peter F. Villano  
*Director of Public Relations*

160 St. Ronan Street, New Haven, Conn.  
Telephone 865 0587

Josephine P. Lindquist  
*Assistant to General Manager*

## **SUMMARY OF ACTIONS COUNCIL MEETINGS Wednesday, May 25, 1966 Organization**

After offering some general remarks concerning the year ahead, and introducing the members of the Council, President Hess declared the floor to be open for nominations for the chairmanship of the Council, 1966-67. Steven J. Martin, Councilor from HCMA, was nominated and, there being no other nominations, was elected to office unanimously.

### **I. Attendance**

Present, in addition to Drs. Hess and Martin, were: Drs. Bradley, Gardner, W. E. Martin, Brandon, H. Caplan, Polivy, Grendon, Egan, Abbot, Spitz, Hastings, Ayres, Ciccarelli, Cramer, Fabro, Grant, Petrie, Pelz, Palomba and Roch. Also present were: Mrs. Lindquist, Mr. Villano and Dr. Richards. Absent were: Drs. Goldberg, Weise, Sr., Rogol, Shepard, Nolan and Wilson.

### **II. Routine Business**

#### **Approval Of Minutes**

As printed and distributed, it was VOTED to approve the minutes of the meeting of April 21, 1966.

#### **Life Membership**

It was VOTED to approve applications for Life Membership received from the following Active Members of the Society:

Eugene F. Kalman, Fairfield (FCMA)

Felix F. Tomaino, Danbury (FCMA)—effective January 1, 1967.

#### **CSMS Dues Exemptions**

It was VOTED to exempt from payment of 1966 CSMS membership dues the following Active Members for the reason indicated:

Stuart L. Joslin, 71 Beach Road, Fairfield (FCMA)—postgraduate education

Charles J. Kallick, 5 Brook Street, Darien (FCMA)—military service

Joseph F. Krivda, 17 Governor Street, Ridgefield (FCMA)—military service

Richard S. Dutton, 7 Woodvale Road, Branford (NHCMA)—Residency training

H. D. Orr, Veterans Administration Hospital, West Haven (NHCMA)—Residency training (beginning July 1, 1966).

#### **Date Of Next Meeting**

The Chairman and the General Manager were directed to call the next meeting at such time as is indicated by the amount of business to be transacted.

### **III. Old, New And Special Business**

#### **Report—AMA Legal Conference, Chicago, April 15, 1966**

Max Caplan, Meriden, filed a report with the Council on the proceedings of this Conference, which he attended as a representative of the Society. It was VOTED to accept the report, with commendation, and to distribute informational copies to all county association presidents and secretaries, also to CSMS legal counsel.

#### **Report—10th National Conference On Physicians And Schools**

Joseph J. Bellizzi, Hartford, filed a report on the proceedings of this Conference, Chicago, September 23-25, 1965, which he attended as a representative of the Society. It was VOTED to accept the report, with commendation, and to distribute informational copies to county association presidents and secretaries.

#### **Report—Committee On Hospitals**

It was VOTED to receive as information a report of the Committee on Hospitals which recommended approval of an AMA Resolution (November, 1965) on the posting of major highways and interchanges with signs designating the location of the nearest hospitals. Since a program of such posting is already well advanced in Connecticut, it was not felt necessary to take further action in this matter.

#### **Representative—AMA National Conference On Infant Mortality**

It was VOTED to authorize the Chairman of the Committee to Study Perinatal Morbidity and Mortality (Samuel D. Rowley, Hartford) to represent the Society at the Conference (San Francisco, August 12-13) and to reimburse him for necessary expenses attendant thereto. It is understood that



Dr. Rowley will prepare and file a report on the proceedings of the Conference with the Council, and that through his report and other mechanisms he will make available to the members of his committee and related committees pertinent information concerning such proceedings.

**Report—Committee On Maternal Morbidity And Mortality**

It was VOTED to approve the report of this Committee, which was a revised series of "Recommendations for the Prevention and Treatment of Toxemias of Pregnancy"; to authorize its publication in the Journal; to authorize the distribution of copies to the Commissioner of Health and to the chief of obstetrics of each hospital having an obstetrical service; and to send a copy as information to the AMA Council on Maternal and Child Care. As has been the case with previous reports of this nature, these recommendations are intended to be used as guidelines for establishing standards for obstetrical procedures, such use by anyone to be made on an entirely voluntary basis.

**Appointment—Ad Hoc Committee On Medicare Experience**

It was VOTED to direct the Chairman to appoint this Committee and name the chairman thereof, as recommended by the Committee on Hospitals and approved by the Council (April 21, 1966). The purposes of the Committee are to: (a) Act as a repository to which practitioners can direct their complaints and problems concerning the management of Medicare and related patients; (b) Advise physicians, whenever possible, how they may deal legally and ethically with such problems; and (c) To study and analyze the collective experience of physicians in treating patients under Title XVIII and Title XIX of P.L. 89-97, with a view to making recommendations to the Council concerning administrative and legislative changes which should be sought from the proper agencies to eliminate recurrent problems and to benefit all parties concerned. The Committee is further expected to take steps to publicize its existence and operation among all members of the Society, and to urge them to submit their problems to it for evaluation, possible advice, correlation and report.

The Chairman appointed the following members to the Ad Hoc Committee:

- Waldo E. Martin, Milford, Chairman (Committee on Hospitals)
- Howard K. Ente, Westport (Committee on Third Party Payments)
- Kurt Pelz, Wallingford (Committee on Aging)

Peter J. Scafarello, Hartford (Committee on Welfare, Finance & Control)

Charles Polivy, Hartford (Member at Large)

John R. Egan, Old Saybrook (Member at Large)

Clifford E. Wilson, Norwich (Member at Large)

**Expression Of Thanks To The Woman's Auxiliary To CSMS**

It was VOTED to convey sincere thanks and appreciation to the Board of Directors of the Woman's Auxiliary to CSMS for the cordial hospitality extended by the Board to members of the Council and headquarters staff at a buffet luncheon served just prior to this meeting. It was further VOTED to inform the ladies of the Board that it will be the Council's pleasure to act as host for a similar "get-acquainted" function in 1967.

**Request—Advisory Committee On School Health**

Held over for final action from several previous meetings, it was VOTED to approve a request of this Advisory Committee (as a compromise to the original request) to publish a one-page newsletter on school health subjects three times a year, such newsletter to be bound as a page in the Journal, and to authorize the Committee to have reprinted sufficient copies of the page to accommodate the needs of the State Departments of Health and Education, the latter agencies to arrange for the distribution of the reprints to interested persons within and allied to their respective Departments. It is understood that the publishing and reprinting costs will be borne by the Society, as a special allocation of funds to the Advisory Committee on School Health through its parent Committee on Public Health.

**Representative To The American College Of Surgeons**

Having been apprised that the American College of Surgeons had scheduled a meeting for June 2, at which it was planned to establish a "Connecticut Chapter" of the ACS to engage in "socio-economic, administrative and legislative activities," it was VOTED to request Charles Polivy, Hartford, to attend this organizational meeting as a representative of the Council, and to subsequently acquaint the Council with the proceedings of the meeting and the plans and objectives of the new organization, if formed.

**Ad Hoc Committee To Study Liaison With Paramedical Groups**

Pursuant to the receipt of informal reports on certain problems being faced by nurses and other paramedical personnel, as a result of the impending advent of Medicare and related legislation, it was VOTED to direct the Chairman to appoint

an ad hoc committee to study and report on the need and/or desirability of seeking to establish liaison with agencies representing nurses and other paramedical personnel, such liaison to be for the purpose of engaging in general discussions of matters of mutual interest and/or concern.

The Chairman appointed the Ad Hoc Committee as follows:

Hilliard Spitz, New London—Chairman  
David A. Grendon, Sharon  
Armando W. Ciccarelli, Bristol

#### **Meetings Of House Of Delegates**

Opinions having been expressed that the April 26 meeting of the House of Delegates had shown appreciable admirable effects of the efforts to "streamline" the proceedings of the House, and that additional efforts might further improve the format, it was VOED to request the Ad Hoc Committee on Administrative Organization and Planning (formerly Ad Hoc Committee on Staff Structure and Function) to study and report on ways by which the efficiency of meetings of the House could be enhanced.

N.B.: *The foregoing is a summary of the proceedings and actions of the Council on May 25, 1966. Detailed minutes of the meeting are on file at 160 St. Ronan Street, New Haven, for perusal by any interested member of the Society.*

#### **PLACEMENT WANTED**

**GENERAL SURGEON** — 33 years of age. Board certified in Surgery and Board eligible in Thoracic Surgery. Connecticut license, military obligations completed. Would like to practice with an associate.

**INTERNIST** — 34 years of age. Board eligible. Would like to form either an association or enter into a group practice either in Hartford or New Haven areas. Available as soon as exchange visitor's status from Canada requirements fulfilled.

**DERMATOLOGIST** — Board eligible, military obligations completed. Would like either to practice with a group or an associate. Available July, 1966.

**OBS-GYN** — Connecticut license. Board eligible, military obligations completed. Wishes to practice with a group or an associate. Available within one month's notice, 42 years of age, married.

**G.P.**—With 2 years training in Internal Medicine, wishes opportunity as associate in Southern Connecticut. Will consider salaried position lead-

ing to partnership or position in Industrial Medicine or a hospital appointment.

**OBS-GYN** — 35 years of age, Board eligible, military obligations completed. Wishes to form either an association with another physician or join a group. University trained.

#### **PLACEMENT OPPORTUNITIES**

**WANTED**—Locum tenens in September for a general practitioner with a view toward permanent association.

**PEDIATRICIAN**—Third Pediatrician to join two other physicians presently practicing in Waterbury, Connecticut. Hospital facilities located nearby in this growing, industrial city.

**PEDIATRICIAN**—Another Pediatrician needed to join a multi-specialty group in New Britain. Board certification or eligibility and Connecticut license or eligibility for licensure required.

**ANESTHESIOLOGIST** — Board certified or eligible Anesthesiologist needed to serve in a 65 bed, fully accredited rural hospital which serves two communities of about 40,000 total population.

**OBS-GYN**—Obs-Gyn associated needed. Board eligible or certified, with essential requirement of speaking French and having military obligations completed. To assume full practice on retirement in two or three years. Located in a large, expanding Central Connecticut city.

**G.P. OR INTERNIST** wanted for full-time or part-time practice with another physician in the Stratford, Connecticut area. No investment necessary. Net income \$25,000 to \$35,000.

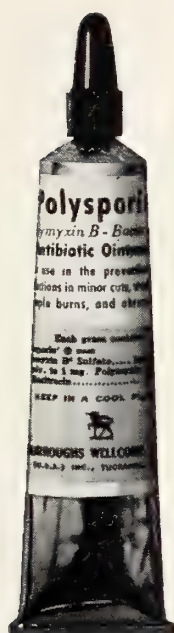
**G.P. OR INTERNIST** to take over practice in Greater Hartford area for cost of equipment only. Will also consider selling just equipment that is in excellent condition. Leaving practice July 1st to go into salaried position.

**MEDICAL EDUCATION DIRECTOR** — Full time Director wanted for 190-bed hospital that is expanding to 400 beds. Salary open. Report to Chairman, Medical Education Committee, Mt. Sinai Hospital, Hartford, Connecticut 06112.

**PSYCHIATRIC RESIDENCIES**—Available in a state hospital. Comprehensive treatment facility for Central Conn. area, associated with Yale University Dept. of Psychiatry and Neurology, which provides supervision in hospital and opportunities for training in areas of special interest. Psychoanalytic training available at Western New England Psychoanalytic Institute. Personal analysis encouraged



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**WANTED**—General Practitioner or Internist for General Medical and Surgical Accredited State Veterans' Hospital. Duties are those of ward officer on a general medical ward. Older physicians are acceptable, many fringe benefits such as housing and maintenance are at minimal cost. Salary range \$13,040 to \$17,040. Apply: Personnel Officer, State Veterans Home & Hospital, Rocky Hill, Connecticut.

ANYONE INTERESTED IN THE ABOVE IS ASKED TO CONTACT THE GENERAL MANAGER'S OFFICE, 160 ST. RONAN STREET, NEW HAVEN, CONNECTICUT 06511.

## 1966 MEETINGS

**September 28** — 41st Connecticut Clinical Congress to be held at Mary S. Harkness Auditorium, Yale University Medical School, New Haven, Connecticut. The program will be devoted to "Recent Advances in the Diagnosis and Management of Liver Disease" and "Recent Advances in the Diagnosis and Management of Thrombophlebitis."

## 1967 MEETINGS

**April 12-13**—Seminar on Hospital Infections in Connecticut to be sponsored jointly by the Connecticut State Medical Society, Connecticut Hospital Association, Yale University School of Medicine, the Connecticut State Department of Health and the Communicable Disease Center of the Public Health Service. No place for meeting has yet been determined.

## THE MIND OF A GENIUS

The ways of genius defy the canons of physiology and medical science. Handel provides an example of the tremendous physical and mental powers of genius. Witness this story. In the summer of 1741—Handel was 56—he was deep in penury and physical suffering. In August of that year he took the manuscript of a libretto which he had received from a flamboyant personage about town, Charles Jennens, and began to study it. It contained the words for a composition to be called *Messiah*. Actually, although Jennens purported to be the author, the words had been selected by an impecunious curate named Pooley who was employed as secretary by Jennens. Handel always believed Jennens was the author; only in recent years has Pooley's share come to light.

Music at that time was running through Handel's brain like a clear-flowing stream. So it was that he set about the composition of what he called *Messiah*, not "The Messiah" as it is sometimes termed. He composed the whole of the first part in seven days; part 2 in nine days; and part 3 in six days. The manuscript shows that the Hallelujah Chorus was composed in less than one day (the two following days were spent in instrumentation.) From beginning to end *Messiah* was composed in 24 days. During the course of this great task Handel's physical state was deplorable. He ate very little, and when his servant, John de Bourk, brought him food, he usually pushed it aside untouched. He did not leave the house but worked all day and most nights by the light of a small oil lamp. All the while he worked at fever pitch, the manuscript showing that his fingers could not set down the notes as rapidly as his brain conceived them. The superhuman energy of the mind seemed to sustain the body in a tremendous feat of creative work.—Scarlett, E. P.: George Frederick Handel: Eyeless in Zion, *Arch. Int. Med.* 113: 889-890 (June) 1964.





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1. Schleif, R.H.: J.A.P.H.A., 46: 179, 1957 \*U.S. Pat. No. 3,062,714

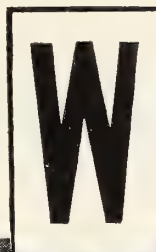
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# Report Of The President Of The Connecticut State Medical Society

## HOUSE OF DELEGATES—ANNUAL MEETING

April 26, 1966

There continues to be criticism that the medical profession has taken too little interest in socio-economic affairs. I believe no group is closer to these affairs than doctors. Connecticut physicians have long exhibited a keen awareness of the interaction between medicine and social progress. Many have directed attention to the need for action in this field. Prominent among others in this effort were Dr. C. E. A. Winslow and Dr. Ira Hiscock who were leaders in the Public Health Services on national and international levels. As early as 1933, in his Presidential address before the New Haven Medical Association, Dr. Samuel C. Harvey, then Professor of Surgery at Yale, presented a scholarly analysis of philosophies underlying the economics of medical care. In summary, he warned physicians "not to rest content but to make changes in their status to meet the changing conditions of society" and that "if medicine is to survive as a profession it must not be on guard but energetically press forward all along the line". This opinion is equally true today.

Last year Dr. Cullen presented an erudite historical review of events leading to the development of the Medicare Bill. The plan for reorganization and realignment of the Health Services under Social Security Administration was conceived in the 1930's in a period of economic depression when doctors drove taxis to eke out a living. It became a major issue under Roosevelt and the New Deal. The long battle over proposed health legislation ensued. In the ranks of the opposition were the large insurance companies, the American Federation of Labor and the A.M.A. who questioned the wisdom and pointed out the hazards of compulsory Social Security-financing. Alternative methods were developed by the Profession to provide aid for medical care of the aged and needy under a voluntary system such as the Kerr-Mills Act, C.M.S. and Connecticut 65 which were pioneer projects in this State. Despite these, and other efforts designed to benefit the people, the Medicare Bill was passed by the 89th Congress during an era of affluence with medical progress at its zenith.

Today, whether we like it or not, the Law has been enacted. We must face the reality and direct our thoughts and energies to the future rôle of the Medical Society in this new relationship between the Profession and the Government. Methods

should be found to accommodate the diverse sectors having vested interests and make it possible for physicians to participate in the administration of the new law. The task may be long and arduous. Medicare is an experimental venture. Its success or failure may well determine the direction of the future of medicine in the United States. As an Association we should continue to seek and demand the highest quality of care, the best professional conduct and the finest kind of service for all Americans.

The first session of the 89th Congress was indeed prolific. In addition to Public Law 89-97, legislation was passed on many fronts. Public Law 89-239 (The Heart Disease, Cancer, Stroke, and Related Diseases Amendments) and Public Law 89-290 (The Health Professions Assistance Act) deserve our close attention. Many other bills included in the package deal—and there will be more—were enacted into law. These pertain to the regulation of certain drugs, extension of health research facilities programs, federal funds for staffing mental health centers, extension of four existing programs of the Community health services act, the medical library assistance act, the vocational rehabilitation act, the clean air act amendments and the water quality act.

Without repudiation of attitudes expressed during the course of the long dialogue and without voicing some strong recriminations, the leadership of the American Medical Association recognized the impact these legislative events will have on the nation and the medical profession acted to adopt methods intending to mitigate the damaging effects and to accentuate whatever beneficial effects there may be in the laws. Six Technical Advisory Committees were appointed, with A.M.A. representation, to help guide the administration in the formulation of regulations and other details related to activation of the law. Thus far, it is said, these representatives have had excellent cooperation and modest success with their negotiation with the Department of Health, Education and Welfare, and, in particular with Secretary John W. Gardner and Mr. Arthur Hess who is directly responsible for administering P.L. 89-97.

Under authorization of the Medicare Law the Federal Government has invaded the field of medical care largely by assuming *financial* support

for certain medical services for those over 65 (Parts A. and B. of P.L. 89-97) and for those other age groups in categories which will be included under Title XIX when adopted. Additional financial support through federal agencies is being allocated for education, medical schools, research, hospitals and other health care facilities. The amount designated for these purposes is considerable (representing some ten billions of tax-dollars, or about one-fifth of the recent annual expenditure for health care). To many this fact poses the threat that the hand controlling the purse-strings will control all.

It would be foolishly presumptuous to predict the future when destiny rests so significantly in the hands of politicians. Never-the-less, the *total* expense which would be incurred in any extension of the plan for Government financing of the amount required for high quality health services for *all* is of such magnitude that it seems unlikely that an enlightened public will readily assume the over-all cost burden on a tax-revenue basis. This seems less possible at a time when the war and defence efforts will inflict an added burden of 65 billions, or more, upon the American people.

The very substantial support by Foundations, the Church, Alumni, Industry and other groups with humanitarian interests, on which there has been great dependence in the past, will continue to be necessary for some time. Likewise there will be a continuing need for voluntary health insurance plans which have proven so beneficial. It is possibly on this type of balanced economic framework of private and government blending of traditional and modern methods of financing that the present level of progress and high standards of medical care can best be sustained. In the words of Secretary Gardner "if the values of freedom are to be preserved, the Federal Government must enter into a creative partnership with the states and cities on the one hand and the private sector on the other". He has called for "a partnership between the Federal Government, physicians, hospitals, universities and health agencies to make a comprehensive attack on health problems".

It is recognized that some measures for the protection of the public welfare in the health field require bold government action to correct problems stemming from pollution of our water and air, the disgraceful toll from accidents on our highways, hazards of quackery and deleterious effects of alcoholism. Cooperative efforts by the Profession and the Government, rather than unilateral legislative action, seem indicated if optimum results are to be attained even in these matters.

The Government, in adopting the technique of disbursing financial aid for health care embodied

in the present Medicare Law, has wisely avoided regulations which will directly curtail the freedom of the physician in caring for his patient. Undoubtedly there are certain limits of tolerance in this respect. The responsibility for the maintenance of high standards of medical service rightfully remains on the Profession with its continuing education and internal mechanisms for the supervision and enforcement of ethical conduct.

Our capacity to provide services at present standards may be jeopardized by the serious shortages in manpower throughout the Nation. Many categories will need augmenting in the near future. It has been estimated that one million additional personnel will be required to adequately implement the proposed program. It is probable that some unequal distribution of personnel exists as a result of the relatively inefficient system based on natural laws of supply and demand. We should seek methods of improved distribution which will bring medical care to all without interfering with the right of the physician to elect the environment of his choice. Furthermore it is important that such measures do not lessen in anyway the motivation of our youth to enter the Profession.

As representatives of the physicians, the American Medical Association, striving to fulfill medical needs and to serve the public, has been constantly working in many areas—education, training, research, and improvement of the clinical application of the highest standards of medical care for the people. It is on the fruits of its energetic endeavors and the knowledge gained by its long experience that all those who would engage in the partnership as proposed might call for advice—or even, on occasion, dissent. Mature and intelligent guidance by its numerous qualified committees is demanded now more than ever before as forces with tremendous potential are joining to mold and shape the patterns of health services in this country.

In the movement to make adjustments in medicine on the American scene much can be learned from critical analysis of the experience of those who have adopted national programs of socialized medicine. Such knowledge may prevent disappointments and deterioration in quality of medical services in this country. It has been said that the American Medical Association should act more aggressively in directing the emerging new patterns for the organization and distribution of medical care. Representing all physicians it should originate and carry out effective programs that serve the Profession and the general population to keep pace with evolving needs. Among others, these programs might be directed toward further education of the public in medical affairs, and the establishment of a nation-wide network of modern communication



facilities to provide consultation and up-to-the-minute educational information for physicians. It must also continue to serve as a forum for discussion as well as decision.

As a member of this federation, the State Society has the responsibility to clarify for itself and the public its position on medical issues and to take positive action when indicated. It might be useful for the State Society, in addition to all its current activities, also to consider the formation of a commission to survey and evaluate the total picture of Health Care and Facilities in Connecticut and supply up-to-date planning guide-lines for the assurance of continuing high quality medical care

for all communities in the State. Every member of the State and County Societies should be encouraged to engage in all medically-related activities at the local levels and to serve on committees or councils dealing with Community health affairs. Physicians, working in concert with laymen on projects where overlapping interests frequently exist, may find resolution for medical problems having important social significance.

We are entering a new era and it is essential that the Profession exert its wise influence in molding effective methods for the betterment of the public health.

ORVAN W. HESS

# TIME OUT . . . *to mark this special day on your calendar*

## SEPTEMBER 28, 1966

### 41st CONNECTICUT CLINICAL CONGRESS

of the

### Connecticut State Medical Society

and the

### YALE UNIVERSITY SCHOOL OF MEDICINE

to be held in

MARY S. HARKNESS MEMORIAL AUDITORIUM — YALE-NEW HAVEN MEDICAL CENTER

333 Cedar Street, New Haven, Connecticut

It will be a one-day program beginning at 9:30 A.M. and adjourning at 5:00 P.M.

### WEDNESDAY, SEPTEMBER 28, 1966

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# WOMAN'S AUXILIARY

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Mrs. Irving H. Krall, West Hartford

*Treasurer*

Mrs. Forest D. Gibson, Farmington

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## OFFICERS 1966-1967

Mrs. Dewey Katz, chairman of the Nominating Committee, presented the following slate of officers for 1966-67 which was unanimously elected at the Annual Meeting, April 27, 1966, Corner House, Farmington.

*President-Elect*

Mrs. Anthony Cipriano  
15 Eastland Road  
Hamden, Connecticut 06514

*Second Vice-President*

Mrs. Edward P. Allen  
505 Ridgeview Road  
Orange, Connecticut 06477

*Corresponding Secretary*

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50 Pilgrim Road  
West Hartford, Connecticut 06117

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Mrs. Henry Sherwood  
195 Old Mill Road  
Middletown, Connecticut 06457

*Recording Secretary*

Mrs. Nicholas Creaturo  
10 Rockland Road  
Trumbull, Connecticut 06611

*Treasurer*

Mrs. Forest D. Gibson  
8 White Oak Road  
Farmington, Connecticut 06032

Mrs. John D. O'Connell, 42 Fulton Place, West Hartford, Connecticut 06107  
was elected in 1965 and installed as President April 27, 1966

The President and Board of the Woman's Auxiliary played host to the President and his Council of the Connecticut State Medical Society at a luncheon on May 25, at the State Medical Building in New Haven. The women met in the morning for their first board meeting, adjourning for the luncheon and then leaving the meeting room to the Doctors. This was the second such meeting. It was thoroughly enjoyed by all, and everyone agreed it should be a yearly event. The ladies and doctors alike, thought President Rosemary O'Connell's "Shrimp Harpin" so unusually good they asked for the recipe—and so we thought is apropos to print it here for all to enjoy. Bon Appetit!!!

### RECIPE

#### SHRIMP CASSEROLE HARPIN

2 lbs. large raw shrimp (1 lb. cooked shrimp equals  
2 lbs. large raw shrimp)  
1 tablespoon fresh, frozen, or canned lemon juice

3 tablespoon salad oil  
 $\frac{3}{4}$  cup raw, regular, or processed rice  
2 tablespoon butter or margarine  
 $\frac{1}{2}$  cup minced green pepper  
 $\frac{1}{4}$  cup minced onions  
1 teaspoon salt  
 $\frac{1}{8}$  teaspoon mace  
Dash cayenne pepper  
1 can undiluted condensed tomato soup  
1 cup heavy cream  
 $\frac{1}{2}$  cup sherry or cooking sherry  
 $\frac{1}{2}$  cup slivered almonds  
Paprika

Early in the day; shell, devein, then cook shrimp in boiling salted water 5 minutes; drain; place in 2 qts. casserole; sprinkle with lemon juice, oil. Meanwhile cook rice as label directions say, drain; refrigerate all.

About 1 hour 10 minutes before serving: start heating oven to 350 F. In butter in skillet, saute, green peppers and onions 5 minutes. Add to

shrimp in casserole, along with rice, salt, and rest of ingredients except, 1/4 cup almonds and paprika. Sprinkle these on top just before serving. Bake uncovered, 55 minutes or till bubbly. Makes 6 to 8 servings.

### **Health Education**

In past years it has been difficult to obtain some type of standardization of health education in our schools. The Connecticut School Health Advisory Council in conducting a survey found that although a few of our communities have excellent health education programs in the public schools, many are woefully lacking.

It was our Auxiliary representative on the School Health Advisory Council who brought to the attention of the members the AMA brochure, "Why Health Education" as an excellent statement of fact. After sub-committee consideration and study, her recommendation that a copy of this brochure be sent to all chairmen of Boards of Education and Superintendents of School with a covering letter signed by the Commissioners of Education and of Health was carried out. With continued effort and interest of the Medical Profession, the Auxiliary and all parents of children in school, it is hoped that a more unified and modernized Health Education program in our schools will result.

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## **AROUND THE STATE**

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### **New Haven County**

#### **Board Of Governors**

#### **New Haven County Medical Association**

Our Board was honored by the attendance of the President of the Connecticut State Medical Society, Dr. Orvan W. Hess, at our meeting on Thursday, May 26, 1966. He was welcomed as the holder of this high office and as an active participant in our County activities.

The agenda was initiated by our Councilor Dr. Frank Abbot's "oral newsletter" of the latest Council meeting.

A report by Dr. James H. Root, Jr., Chairman pro-tem of the Third Party Review Committee dealt with the meeting of this committee held in Waterbury on May 18th. Ground rules for their future guidance were set up. These were thoroughly discussed. The Board voted to commend the committee for its efforts.

Dr. Max Caplan, our President, reported on his attendance in Chicago as Delegate from New

Haven County to the meeting called by The Congress of County Medical Societies to deal with recent developments in the Medicare program. A full and very complete copy of these activities has already been mailed to all members of our County Association which was edited by Dr. Caplan. The commendation of the Board has been repeated by individual members as expression of appreciation for this information.

After routine matters were attended to, the meeting closed with adjournment for the usual social hour and dinner.

Respectfully submitted

H. A. LEVIN, M.D., *Clerk*

### **One-Millionth Recipient**

The Department of Health, Education, and Welfare, Social Security Administration announced that Marlin Enders, the one-millionth disabled worker in current pay status was recently added to the disability benefit rolls under the Social Security disability insurance program.

This figure represents a total payment of \$125 million a month to disabled workers, disabled children, and other dependents of disabled workers. Connecticut's recipients number 11,343 through December 1965, and this represents \$1,162,948 a month in payments.

This milestone is significant because it focuses national attention on the new definition of disability and on the scope of protection the program now provides.

Mr. Enders, the one-millionth recipient, a 51 year old coal miner, was awarded disability benefits totaling \$263.50 a month for himself and his family. He was allowed under the new definition of disability impairments lasting 12 months or longer. His claim would have been denied under the old definition that required a prognosis of long and indefinite duration.

Since the "wage freeze" in 1955, the program has come a long way. In 1957, the first cash benefits were paid to older disabled workers . . . age 50-64. Later the minimum age requirement was dropped, a disabled child provision was added, and benefits were provided for certain dependents of disabled workers. The 1965 amendments brought the program's first change in the definition of disability.

FRANK H. COUCH, M.D.

*Chief Medical Consultant, Bureau of Disability Determination, Division of Vocational Rehabilitation, Connecticut State Department of Education.*



## News From Yale University School Of Medicine

Dr. Albert Jay Solnit, a prominent authority in the fields of child psychiatry and psychoanalysis as well as comprehensive pediatrics, has been appointed Director of the Yale University Child Study Center.

The appointment, effective July 1, 1966, was announced by President Kingman Brewster, Jr., of Yale.

Dr. Solnit, a Professor in both the Pediatrics and Psychiatry departments of the Yale School of Medicine, succeeds Dr. Milton J. E. Senn who has directed the Center since 1948. Dr. Senn, 64, will continue at the Center as Sterling Professor of Pediatrics and Psychiatry, and will devote his entire time to teaching and research.

The Yale Child Study Center is the successor to the Yale Clinic for Child Development, founded in 1911 by the late Arnold Gesell, noted pioneer in child behavioral science. Dr. Gesell headed the Clinic until his retirement in 1948, at which time the Clinic's functions were taken over by the newly-established Child Study Center.

Staffed by pediatricians, psychiatrists, psychologists, educators, and social workers, the Yale Child Study Center is famous for its research and teaching programs as well as its clinics for infants and children.

Dr. Solnit, a member of the Yale medical faculty since 1949, is known for his work and writing on child development and mental health. He is Chairman of the Committee on Child Analysis of the American Psychoanalytic Association and this year completed a three-year term as President of the Western New England Institute for Psychoanalysis. He is currently a training and supervising analyst in the Institute.

As psychiatric consultant to the New Haven and North Haven public school systems and to the pre-kindergarten school program in New Haven, Dr. Solnit works closely with community educators. He is also Chairman of the Psychiatric Council of the Elm Haven Concerted Services Program, and a member of the New Haven Community Health Services Committee, the Research Advisory Council of Community Progress, Inc., and the South Central Connecticut Regional Mental Health Planning Council.

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## Special Notices

### COURSE IN POSTGRADUATE GASTROENTEROLOGY

October 27, 28, 29, 1966

The Annual Course in Postgraduate Gastroenterology of the American College of Gastroenterology will be given at the Bellevue Stratford in Philadelphia, Pa., 27, 28, 29 October, 1966.

The Moderators for the Course will again be Dr. I. Snapper, Consultant, Ft. Hamilton Veterans Administration Hospital, Brooklyn, N.Y. and Dr. John L. Madden, Clinical Professor of Surgery, New York Medical College and Director of Surgery, St. Clare's Hospital, New York, N.Y.

The faculty for the Course will be drawn from the Medical Schools in and around Philadelphia. The subject matter to be covered, from the medical as well as the surgical viewpoint, will be essentially, the diagnosis and treatment of gastrointestinal diseases and comprehensive discussions of diseases of the esophagus, stomach, pancreas, liver and gallbladder, small intestine and colon. A session on instrument technics will be held at the Albert Einstein Medical Center, Northern Division.

For further information and enrollment, write to the American College of Gastroenterology, 33 West 60th Street, New York, N.Y. 10023.

**DOCTOR—Does your wife like to read  
the Auxiliary news? Then be sure and take  
your copy home.**

## SPECIAL REPORT ON AMPAC NATIONAL WORKSHOP

Washington, D. C.—May 21, 1966

*At the Council meeting of May 25, 1966, it was voted to publish the following report for the information of members of the Society.*

The National Workshop of the American Medical Political Action Committee (AMPAC) was held in Washington, D. C., on May 21, 1966. Since the meeting took place in the nation's capital, those attending had opportunity to hear and talk with several members of Congress and were greatly encouraged to learn of how valuable the latter consider AMPAC to be—to themselves, and to their respective parties. Democratic and Republican spokesmen alike expressed the opinion that AMPAC has become increasingly important in the field of political education and action, and Mr. Jack Mills, Republican Congressional Committee Director, said he felt that AMPAC was perhaps *the* most effective group helping to elect good candidates put up by his party.

During the sessions on candidate selection, on methods of working with candidates and their organizations, and on the elements of waging a successful congressional campaign, emphasis was placed time and again on the recognized effectiveness that AMPAC is demonstrating in all these areas of political activity.

The final speaker of the Workshop, Representative Melvin R. Laird (R.-Wis.), explained to the audience how necessary he felt the work of AMPAC will be this year and in the years ahead. He stated that many important bills that were enacted into law by the 89th Congress went through with Democratic majorities of only twelve votes, and that if only seven of these seats had been held by Republicans much of this legislation would have been defeated or substantially curtailed. As a member of the House Appropriations Committee, it is his considered opinion that the total impact of most of these bills already passed will be dependent on how much money is authorized for their implementation, and that the funds have yet to be appropriated. Hence, even though the laws are on the books, the selection and election of fiscally conservative candidates in 1966 are of vital importance and call for even greater campaign efforts in the months ahead.

Congressman Laird reported on a recent poll which indicates strongly that a great many voters are becoming thoroughly disenchanted with the

way things are being done in Washington today, and concludes that a minimum of thirty-one House seats may be in jeopardy. If unseated, he said, the incumbents (mostly Democrats) must be replaced by legislators more favorable to the views of Medicine and like-minded groups, and he stressed that only political action agencies like AMPAC have the time, money, organization, know-how, and workers to bring these needed changes about.

He spoke of the critical financial situation which has been allowed to develop in New York, where the implementation of Title XIX of P.L. 89-97 (signed into law on April 30) will make more than 7 million of the State's 18 million residents eligible to receive practically unlimited, "free" (tax-supported) hospital, medical, dental and nursing care. So liberal is the program that families of four with a net income (after taxes and health insurance premiums are deducted) of up to \$6,000 a year and up to \$3,000 of savings can qualify to receive comprehensive health services at public expense. The Congress has estimated that the total Federal contribution to implement Title XIX *nationwide* would not be more than \$238 millions, and yet now it finds New York State alone asking for \$207 millions as its entitled "share." The funds appropriated by Congress, the speaker said, are obviously insufficient to satisfy the first-year demands of seven states for Title XIX programs, let alone those of the entire fifty.

Over and over again, the Workshop emphasized that the "dream" of social legislation and the "reality" of its financing are two quite different things, and that 1966 and the next few years will constitute a period in which physicians (among others) will have an opportunity to try to reverse the unwise course that "me-too" legislators have set for the country. If AMPAC does its job—and does it well—perhaps a halt can be called to the current trend wherein the Administration calls an executive tune to which its adherents in the legislature are expected to dance dutifully—with practically no opposition, and after the least possible amount of public debate.

Respectfully submitted,

MAX CAPLAN, M.D., Meriden



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## OBITUARY

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### **Edward J. Blumenthal, M.D.**

**1907 - 1966**

Edward J. Blumenthal died on April 24, 1966 at the age of 58 at his home in Ansonia.

He was born in Ansonia, son of the late Samuel and Sarah Rose Blumenthal of Ansonia and nephew of the late Herman J. Blumenthal, Yale Medical School, 1921, of Brooklyn, New York. He attended Ansonia public schools and the Yale Sheffield Scientific School from which he was graduated in 1928. Following this he was awarded his



doctorate of medicine at the Long Island College of Medicine in 1932. Following internship at Grace Hospital in New Haven he engaged in general practice, with a special interest in anesthesiology, from his office in Ansonia which he continued over a period of thirty years.

During World War II he served in the United States Medical Corps with the rank of Major in the 48th Portable Surgical Hospital in the China-India-Burma theatre of operations for 26 months.

He was a past president of the Naugatuck Valley Medical Society, past president of the Griffin Hospital Medical Staff, a member of the American Medical Association, a member of the American Society of Anesthesiologists, The American Academy of General Practice, the Connecticut State Medical Society in which he served as New Haven County delegate to the State Medical Society. He was also a member of the editorial board of the State of Connecticut *G.P. Journal*. He was a mem-

ber of the Beth Israel Synagogue Center in Derby, Connecticut.

Dr. Blumenthal leaves his wife, Adele Cohen Blumenthal, a daughter, Elaine T. Blumenthal, a son, Joel M. Blumenthal, three brothers, B. Sidney Blumenthal of Ansonia, David Blumenthal of Orange and Dr. Irwin S. Blumenthal of Santa Monica, California; two sisters, Mrs. Seymour Jacob of Skokie, Illinois and Miss Miriam Blumenthal of Ansonia and several nieces and nephews.

He was a dedicated physician with a forthright sincerity and steadfastness that served as a great bulwark to all who knew him. His life was crowned with a host of devoted friends and patients. His genuine and clarifying helpfulness was much sought after. He was a boon to his community and to society at large. He will be sorely missed by those he has left behind.

Blessed be his name and his memory!

VICTOR L. SZANTON, M.D.

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## In Memoriam

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**Kirby, Sam B.** — New Haven; Yale University School of Medicine, 1928. Dr. Kirby practiced medicine in New Haven for over 30 years. During World War II he was in charge of the 60th General Hospital in the Philippines as a lieutenant colonel. Dr. Kirby was also a member of the Military Order of World Wars. He was a member of the New Haven County Medical Association, the Connecticut State Medical Society, the American Medical Association, and the Yale Club of New Haven. Dr. Kirby died June 1, at the age of 62.

**Konopka, Frank J.** — Wallingford; Georgetown University School of Medicine, 1931. Dr. Konopka had practiced medicine in the Wallingford area for over 25 years. During World War II, he served in the United States Air Force as a captain for four years. He was a member of the Meriden Hospital medical staff, the New Haven County Medical Association, the Connecticut State Medical Society, and the American Medical Association. Dr. Konopka died May 22, at the age of 60.

## 62ND ANNUAL CONGRESS ON MEDICAL EDUCATION

Chicago, Illinois — February 3-8, 1966

The 62nd Annual Congress on Medical Education of the American Medical Association was a very interesting and stimulating meeting in that its agenda included lengthy discussion of many of the most serious problems confronting American medicine at the present time, problems that will continue to beset us all that will require solutions in the decades to come.

Population growth and change, and the problems these will pose for medical education, provided the subject matter for the lectures on the first morning of the Congress. Dr. Mevill, of the U.S. State Department, addressed the Congress, and his remarks and statistics were an unanswerable rebuttal to those who deny the existence of a "population explosion" or who are able to rationalize this by reference to previous centuries or by entirely unwarranted optimism that all can be coped with. The problem is an exceedingly complex one, and its future influence on virtually all human affairs, social, economic, etc., as well as medical, cannot be underestimated and should be of tremendous concern to all thinking men. Although in medicine our focus is on the individual, we nonetheless cannot be blind to the effect that this appalling increase in population is having and will have more and more on those whom we care for medically and on the practice of medicine itself.

In 1900 the human population of our globe was estimated to be slightly over a billion. By 1920 this figure had risen to approximately two billion. Now, despite World Wars and other catastrophes that have taken a huge toll of human life, it is estimated that we have over three billion souls on this planet, a number that, it is thought on the basis of current trends, will escalate to seven and one-half billion by the year 2000.

Some facts regarding the potentially disastrous effect of this increase in the world's population may be sobering. Until recent years there always has been a supply of land reclaimable from the standpoint of agricultural pursuits. This supply is now well-nigh exhausted. In Asia, apparently, it is already exhausted.

Of interest, also, is the disproportionate rate of population increase among countries. The so-called "developing nations" (i.e., the countries of Asia and Africa) show a much larger rate of gain than do the "developed countries" of Europe and North America. South America shares this rapid increase with Africa and Asia. And it is predicted that in

the next fifteen years, India, already over-burdened will have an increase in population equal to the present census of the United States.

And, meanwhile, in all of these areas great efforts are being made to increase per capita income and to achieve economic improvements; obviously, all such efforts are nullified completely by the high birth rate.

All this is compounded by the high morbidity rates. True, thanks to modern medicine, mortality rates have declined sharply, but morbidity rates have not. These have, perhaps, even increased because of the greater number of people, the burgeoning congestion of their living, and, most important, because of the increasing malnutrition.

Some national demographic trends in this country are having a definite effect on the changing medical needs of our communities. One of the most important of these is the rapid rate of urbanization of our population because of increasing industrialization of the economy. In 1800 6 per cent of our population lived in cities— the figure in 1960 was 70 per cent! It is said that two per cent of our land area contains 70 per cent of our people! Therefore, there has occurred a definite geographic re-distribution of our population as well as an astronomical increase in its size. There has been a great increase in two age groups, the children and the elderly, both partially because of improved medical care. Since 1750 there has been a steady decline in death rate, and there has been no recent change of statistical importance, so birth rates are more important in determining and predicting population size. There is some racial change in proportion of population, as the Negro birth rate has been higher than the white, although this is expected to level off in the years to come. Despite our population increase, however, it is interesting to learn that twenty-four countries, including the Soviet Union, have a lower infant-mortality rate than we do. In fact, our rate is double that of Sweden.

Some of the above facts have forced changes upon medicine. Urbanization (and the subsequent flight to the adjacent suburbs) has depopulated much of some sections of the country and has led to a decline in rural medicine and the increase in hospital, group, and clinic type of practice. The population increase, especially in age groups like the very young and the very old, who need more



medical attention, has placed greater burdens on the shoulders of practitioners of medicine.

We are now unhappily involved in a race between economic production and human reproduction such as the world has never witnessed before. This is probably the number one problem of the world now. It is difficult for most human beings to envisage situations that they have not remotely experienced themselves. Therefore, the possibility that many of our descendents may have only one square foot of ground to live on may seem fantastic to many. Since this has never happened, it couldn't possibly happen—But it could, and may—unless we start to do something about it immediately. To procrastinate may be disastrous, and the picture presented by statistics is already frightening.

We of the medical profession have a definite responsibility in this area. It will be our task to try to limit this trend, perchance to reverse it somewhat, both at home and abroad. Realization of this weighty responsibility is reflected by our government's change in attitude about the dissemination of birth-control information in foreign countries.

In many countries programs for birth control are now in operation. Much has been done in Korea, India, Taiwan, but the surface has only been scratched because of the magnitude of the need.

An area surveyed in Thailand gives us an example. In this locality the average family had four children, wanted no more. Only one per cent of the women had used contraceptives. When first questioned, 60 per cent of the women were interested in contraception, wanted help. Now 90 per cent request it.

Although it is manifest that population control can be achieved only by birth control, there are definite factors militating against regulation of fertility. Superstition, ignorance, taboos of primitive peoples, religious objections, the feeling of husbands that one's virility is proved by the size of one's family, etc.—all these, cultural factors all, can sometimes be an impediment to acceptance of principles of limitation of family size. In some underdeveloped countries in which health care and social agencies are all but lacking but in which child mortality is high, having many children is the only way to insure ones old age—some may survive to take care of the "old folks." Another factor that impedes success is the lack of trained personnel, medical and paramedical, to do the work regardless of a nation's desire for contraceptive help.

It is the responsibility of physicians to learn the various techniques of contraception and to advise and help their patients in this very important facet

of medical care. *This is a matter of responsible medical practice.* The suitability of method must be decided for each individual patient and, in addition to obvious medical indications and contra-indications, her motivation must be taken into consideration in the final decision.

Some figures given by one of the speakers were somewhat alarming and will be shocking to many readers, *viz.*: 1/6 of brides pregnant when married; 1/3 of high school brides pregnant when married; 1/2 of teen-age marriages end in divorce; 40 per cent of illegitimate births in this country are in teen-agers!

Good premarital and marital counseling in all age groups is paramount in importance and training for such duties should start in medical school, where there should be a course covering the whole range of problems that revolve around reproduction. Socio-economic factors and their effect on families and their health, mental and physical, should be studied, as well as fertility control, nutrition, genetics, child-rearing, and so on. And the sequela of poor care, such as maldevelopment and behavior disorders and maladjustments, should be brought out to the student. Sexual advice to teen-agers should not be neglected. In other words, a multi-disciplinary approach, involving biological and social sciences, could form the basis for a course in human reproduction (and who is more concerned with this subject than physicians?) and would weld into one course some of many things, such as anatomy, obstetrics and gynecology, pediatrics, psychiatry, and social-worker experience.

Adequate premarital counseling is advocated, as sexual and marital maladjustment of parents can be not only disastrous to their marriage but catastrophic for their children. If the bride-to-be is in her teens, advice to postpone the first pregnancy until after she is twenty years of age is wise. If, however, she has reached her twenties, appropriate advice from the standpoint of marriage stability would be that she wait six to twelve months before voluntarily conceiving. Postpartum advice regarding contraception and size of family is the obstetrician's responsibility. Child-spacing is important for family economics, health, and stability, and reducing the goal from 4-5 children to 2-3 is suggested for better family situation as well as for its role in curbing the huge increase in population.

Advice and contraception are certainly to be preferred to abortion and divorce.

The afternoon of the first day of the Congress was devoted to several papers on medical education. Some important conclusions were brought out, and they are worthy of being pondered a bit, as they are not completely in accord with long-held

beliefs on the subject. One was that the size of the class had no effect on the quality of the education. Another statistical conclusion was that the curriculum seemed to have no effect on the choice of a career, and, perhaps the most explosive and thought-provoking fact was that grades in medical school do not necessarily correlate with later competence in the practice of medicine.

Interest has been aroused in so-called "comprehensive medicine." This term includes specialty care with "health-team" aid and with consideration of all economic and social factors pertinent to the patient.

What constitutes an "adequate learning setting" for would-be physicians? This was discussed at length and seems to depend on the type and size of house staff and faculty and the amount of faculty supervision.

Demands are increasing quantitatively for medical graduates, demands which are difficult to assess because of new medicine programs, but quality is the goal of medical education. Criteria of patient care, evaluation of such care (as determined by self-auditing by physicians), preparation for the study of medicine, and house-staff were all discussed.

Another subject was "Education for Family Practice." Although general practitioners are decreasing in number, the American Medical Association believes that the family practitioner plays an important role in medicine and is important to national health. Committees have been formed to study this subject.

Breadth of comprehension rather than depth in particular fields may well be the training of choice for those entering family practice, and studying patients in varied settings, such as in their homes or in nursing or convalescent homes as well as in the hospital, may be good training for the student. The need for flexible programs was stressed.

Issues in graduate medical education were discussed next and the discontinuity in the educational process was said to be the over-riding issue in medical education especially in the graduate group. It was felt that the traditional premedical courses in college, medical school, and post-graduate training in a teaching hospital constituted a program often guilty of lack of co-ordination and correlation but often characterized by duplication and waste of time. Teaching, it was felt, should be done by a group rather than by one man. The old apprenticeship system was thus under fire, regarded as an anachronism, as its result hopefully was that the apprentice's knowledge and skills would equal those of the master. This, it is thought, is no longer suf-

ficient in the progress of medicine—he should *exceed* the master!

A National Academy for Continuing Medical Education is being founded, and a large pilot project is being conducted in Utah. The development of the curriculum for such a postgraduate education must be based on three factors: patient needs, physician performance, and medical knowledge. In this program the physician makes an individual assessment of his new needs in knowledge based on his own type of medical practice and his performance in handling it. Decisions will gradually be made, evolving from experience, as to development of a faculty for this type of project, the teaching techniques to be used, and the modes of communication with the physician-learner.

The second morning of the Congress was devoted to the many facets of the subject *Measurements of Medical Competence*.

Various intramural measurements of student learning were discussed at length. For example, the traditional "compartment courses" (that is, separate courses in each subject concluded by a separate examination in each one) was attacked, as it was felt that these don't evaluate the student in many ways. "The possession of facts is less important than their application" seemed to be a key-note, but don't we have to possess facts before we can apply them? Much time was wasted in truisms, such as "not everything we count counts, and not everything that counts can be counted."

The value of the comprehensive examination, to stress the unity of the past and of the whole, was the subject of one of the lectures. In another, the concept of "pre-testing" was discussed—i.e., that of testing the knowledge a student already possess before he starts a formal course. Comparison of the grade on such an examination with that on a final test tells much more about a student's progress rate and learning ability than does the final grade alone.

In one medical school the personal "follow-up" of each clinic patient by a senior student is being tried out. After the initial work-up in the general clinic, the student assigned to the patient then follows him, literally, to any specialty clinic to which the patient is referred, participates in examination, and learns treatment prescribed; he becomes, so to speak, the patient's general practitioner. He is evaluated on his day-to-day performance. It has been found, however, that such grades do not necessarily correlate with those he receives on his final examinations. The question is therefore logically raised as to which set of grades is the more accurate as a predictor of the student's later performance in the practice of medicine. Examinations of all sorts do not evaluate many traits, such as kindness, sym-



pathy, desire to learn and cooperate, and ability to inspire confidence. Systematic bedside teaching of interns and residents by attending physicians is urged.

Medical competence and its evaluation were discussed in another paper. It was felt that there existed three methods of such appraisal—i.e., (1) knowledge and skills (as determined by examinations of all sorts); (2) methods of practice (discovered by examination of records, medical audits and direct observation of the physician at work, in office and in hospital; and (3) end results (the outcome of treatment).

There are obvious difficulties inherent in the above-listed methods of evaluation. Number one brings up again the question of the relationship of proficiency in tests to competence in practice, and number three involves all sorts of comparisons with many variables (age and sex of patient, nature and stage of disease process, and so on.) Such varying factors obviously make it difficult to establish criteria for evaluation of the end-result. Perhaps the patient's own appraisal of his treatment should also be considered.

Various factors leading to life-long medical competence were cited. Chief among these were medical academic ability (class rank), results of vocational tests, type and length of hospital training, associations, and experience (volume of practice). The relative lack of training in doctor-patient relationship was deplored, and the great influence (good and bad) of medical faculty on subsequent careers of their students was stressed.

The role of external examinations (tests given outside of the medical-school curriculum, such as boards of various sorts) was then discussed. It was felt that often such examinations shape teaching methods in institutions. Although multiple-choice tests give a wider distribution of grades than do the essay-type of examinations, more students pass with the former type of quiz. However, the former type is much easier to correct, and the man-hours needed to grade essay-type examinations seem to preclude their use.

A discussion of State Board Examinations followed. It was pointed out that the Boards of Medical Examiners are governed by the statutes of the several States, and it was felt by one speaker that they were at times too much pre-occupied with legal matters and not sufficiently with examinations. There has been a lack of uniformity in the standards of different Boards. In 1962 twenty-six states passed all "native sons." Three State Boards did not fail a single candidate in ten years, and nine states passed over ten thousand candidates,

failing only fourteen. The old question of an Examination Center of the Federation of State Medical Boards to provide a pool of examinations for use by all states was raised. This could, it was felt, lead to uniformity of examination standards and eventual universal endorsement of successful candidates by all states.

The National Board examinations were then discussed and the ever-enlarging role they play in the country was proved by statistics. Not only are more and more candidates for licensure taking them, but many State Boards use part or all of the National Board examinations in testing their applicants, and forty-six medical schools have made the National Boards part of their curriculum, requiring all students to take them. Special examinations have been prepared for some schools to help in the evaluation of new teaching methods. In addition, testing of interns in military hospitals and preparation of examinations for the various specialty Boards has been done by the National Board.

Brief mention of the Boards of the different specialties was made and of their part in higher medical education.

Many factors are creating a crisis in American medicine. There is a shortage of doctors, and an ever-increasing demand for medical services is developing because of population growth, urbanization of the country, the growing affluence of the community as a result of decreased unemployment and tremendous economic growth, our commitment to international health, "Medicare," and the present needs, civilian and military, in Viet Nam.

Means of increasing the physician population of the United States were discussed, such as the expansion of existing medical schools and the founding of new ones. The help planned by the Federal Government (i.e., matching funds, construction grants) in the program were brought out. The ratio of doctors in the population and the fact that 1200 more medical students will be needed by 1975 were mentioned. At present, the attrition rate of medical students in this country is 12 per cent, a rather large figure. Better selection of students, increased financial assistance to the candidates for the M.D. degree (it is already being given to candidates for the Ph.D. degree involved in research, but not to medical students!) and the greater use of M.D.'s on pre-clinical faculties were stressed as important in decreasing this rate of attrition. At the moment, the preclinical faculties of many schools consist mainly of Ph.D.'s, and these men, by their teaching and grades in the first two years, are deciding which men are going to be given the chance to be physicians. This state of affairs reflects back to the

college campus and influences choice of career among undergraduates.

The country-wide nursing shortage has also increased the "doctor demand" in that it has placed an extra burden on the individual physician in terms of patient care. It is suggested that an experimental program instituted at Duke University, that of recruitment and training by doctors of young men to be doctors' assistants, may help to solve the problem of shortage and paramedical personnel. Not only the recruitment, but also the training and remuneration of these men, who will be known as "doctor's assistants," will be performed by physicians. These recruits will be similar to the trained Medical Department enlisted men of World War II; they will perform laboratory tech-

nicians' duties, will act as nurses, will help the doctor in both office and hospital, but will be paid by the doctor, not the hospital.

The need for greater medical faculties in the future is obvious. Part of this need should be filled from the rejuvenation of the part-time faculty concept.

Much of the remainder of the talks merely re-emphasized the need for greater evaluation of the standards in medical schools and house-staff training. The necessity for physician evaluation, for training of more general practitioners, and for more physicians for the future were all again re-stressed in various ways.

Respectfully submitted,

CHARLES B. CHENEY, M.D.

### The Definition Of Life

The definition of life is usually sought for in abstract considerations; it will be found, if I mistake not, in the following expression:—Life consists in the sum of functions, by which death is resisted.

In living bodies, such in fact is the mode of existence; that whatever surrounds them, tends to their destruction. They are influenced incessantly by inorganic bodies; they exercise themselves, the one upon the other, as constant an action: under such circumstances they could not long subsist, were they not possessed in themselves of a permanent principle of reaction. This principle is that of life; unknown in its nature, it can be only appreciated by its phenomena: an habitual alternation of action and reaction between exterior bodies, and the living body, an alternation, of which the proportions vary according to the age of the latter, is the most general of these phenomena.

There is a superabundance of life in the child: In the child, the reaction of the system is superior to the action, which is made upon it from without. In the adult, action and reaction are on a balance; the turgescence of life is gone. In the old man, the reaction of the inward principle is lessened, the action from without remaining unaltered; it is then that life languishes, and insensibly advances towards its natural term, which ensues when all proportion ceases.

The measure, then, of life in general, is the difference which exists between the effort of exterior power, and that of interior resistance. The excess of the former is an indication of its weakness; the predominance of the latter an index of its force.—Bichat, X.: *Physiological Researches on Life and Death*: 1800, F. Gold (trans.), London: Longman, Hurst, Rees, Orme, and Browne, 1815.



# RECOMMENDATIONS FOR THE PREVENTION AND TREATMENT OF TOXEMIAS OF PREGNANCY

## Prenatal Routine

### I. Prophylaxis

A. Frequency of patient's visits to physician through prenatal course.

1. A minimum of one visit every four weeks up to 28 weeks.
2. A minimum of one visit every two weeks from 28 to 36 weeks.
3. A minimum of one visit every week from 36 weeks to delivery.

B. Content of first visit.

1. Complete history and physical examination.
2. Complete urinalysis.
3. Blood group and Rh determination.
4. Instruction as to diet and weight control.

C. Content of each subsequent visit.

Each visit should include as minimum:

1. The recording of blood pressure and weight.
2. The testing of urine for albumin and sugar.
3. The questioning of patient regarding symptoms of edema, headache, epigastric pain, blurring of vision.
4. Instructions as to diet. Sodium restriction (eliminating salty foods, table salt, and baking soda), high protein, high mineral high vitamin.
5. Check on weight control—gain of no more than two pounds per month. Total weight gain of no more than 20 pounds over *ideal* weight.
6. Special attention given to abnormalities. More frequent visits for patients with essential hypertension, diabetes, urinary disease and previous toxemias. Obstetrical consultation is desirable in such cases because of their tendency to develop toxemia.

### II. Management of the office patient who shows:

A. Excessive weight gain.

1. Diet, low sodium, high protein, mineral and vitamin. Have patient tabulate diet for one week and submit the same. Diuretics may be considered.
2. More frequent visits.
3. Hospitalization if uncontrolled.

B. Hypertension.

1. Blood pressure 140/90 or over, or rise of diastolic of 10 or more, or a systolic of 20 or more.

2. Check urine for infection (culture clean catch specimen).
3. Diet, low sodium and high protein.
4. More frequent visits.
5. Rest at home.
6. Sedation.
7. Report headache, edema, epigastric pain or blurring of vision at once.
8. Hospitalization if not controlled.
9. If in doubt, have obstetrical consultation prior to admission.

C. Edema of face, hands or feet.

Treatment same as for excessive weight gain.

D. Albuminuria.

Treatment same as for hypertension.

E. Hospitalization should be urged if:

1. In spite of good conservative treatment weight continues to increase excessively.
2. Elevated blood pressure continues (140/90) or blood pressure continues to rise in spite of good conservative treatment as outlined.
3. Persistent edema together with unusual weight gain.
4. Albuminuria continues to be present or is increasing in amount.

F. Patients reporting any of the following symptoms *should be seen immediately*:

1. Severe headache.
2. Sudden edema, particularly of the face.
3. Epigastric pain.
4. Blurring of vision.

G. Immediate hospitalization if there is:

1. Sudden rise in blood pressure (such as 160/100).
2. Evaluate other symptoms and if due to toxemia, admit.
3. Convulsion.

H. Early hospitalization of toxic patient is of paramount importance in preventing more severe or even fatal progress of this disease.

## In-Hospital Procedures

Upon admission to hospital toxemia routine should be started and consultation rules adopted by the hospital should be adhered to. It is strongly recommended that wherever toxemia patients are being treated, a special toxemia tray containing necessary emergency drugs and IV solutions be readily available.

A. If patient is pre-eclamptic upon admission to hospital:

1. Treat conservatively for 24-48 hours or longer.
  2. If patient is not near term and good results are being obtained from conservative treatment, ideally continue hospitalization. If patient becomes sufficiently improved, patient may be seen in doctor's office at least twice a week. Treat conservatively until baby is viable or as long as possible. If it is apparent that conservative treatment is failing, re-hospitalize patient.
  3. Toxic patients must be seen frequently by nurses and doctors.
  4. If patient is at or near term, consider delivery:
    - (a) Whether multipara or primigravida, induce if possible.
    - (b) If induction in either case seems impossible or is unsuccessful, Caesarean section should be considered.
- B. Toxemia with convulsions (eclampsia) should be treated conservatively until controlled. Then deliver by the most feasible method. Avoid Caesarean section if possible. Consider induction by oxytocin drip and rupture of membranes.

#### **Toxemia Routine For Hospitalized Maternity Patients**

1. Consultation recommended.
2. Single bedroom if possible and no visitors.
3. Complete bed rest.
4. Weigh patient on admission and daily.
5. Record intake and output.
6. Low sodium, high protein diet.
7. Blood pressure, temperature, pulse, respirations, and fetal hearbeat every four hours.
8. Clean catch urine on admission for routine analysis and culture; daily clean urine thereafter for routine analysis.
9. Blood chemistries
  - (a) Draw blood on admission for BUN, Creatinine, uric acid, total serum protein, CO<sub>2</sub> combining power, sodium, potassium chlorides and blood sugar.
  - (b) Repeat chemistries as indicated.
10. Hematocrit and hemoglobin on admission.
11. Sedation.
12. At least one 24 hour urine for total protein if 3+ or 4+ albuminuria is present.

#### **Important**

It must be clearly understood that no routine will cover all pre-eclamptic patients. The above routine is merely intended as a guide. It will be modified for the patient who is responding satis-

factorily—and will be changed somewhat for the patient who is not improving—and, of course, must be modified drastically for the patient who is a severe toxemia with imminent convulsions or has already convulsed. It is most important (a) that the toxic patient both before and after delivery be watched carefully even though she may appear to be improving (her condition may change quickly); (b) that a competent consultant accept the responsibility for the patient's care.

#### **Postpartum Toxemia Routine**

It is assumed that there are routine postpartum orders in each hospital licensed by the Connecticut State Department of Health to take care of obstetrical patients.

Treatment of the postpartum toxic patient cannot be made a routine except in principle. The first forty-eight hours postpartum, and particularly the first eight hours, are the most critical.

It must be remembered that in the care of postpartum toxemia, pre-eclampsia or eclampsia that (1) it may develop for the first time postpartum, (2) pre-eclampsia may be made more severe by labor or may progress into eclampsia. With this in mind, the following recommendations are made.

#### **I. Urine.**

- A. Test urine taken at time of delivery for albumin immediately.
- B. Examine subsequent urines for albumin daily if signs of toxemia persist.
- C. Obtain clean catch urine on the third day postpartum for urinalysis and culture (in order to detect pyelonephritis).

#### **II. Blood Pressure.**

Take and record blood pressure:

- A. Immediately following delivery.
- B. Then every half hour for two hours.
- C. Then every one to two hours for six hours.
- D. Then q.i.d. until discharged.

#### **III. Medication.**

- A. Continue medication postpartum under consultant's orders.

#### **IV. Activity.**

- A. Continue with complete bed rest until patient is ordered up by physician.

#### **V. Intake and output.**

- A. Record intake and output until discontinued by physician.

#### **VI. Blood chemistries—repeat as indicated.**

#### **VII. Diet.**

- A. Continue low sodium diet postpartum until signs of toxemia have disappeared.

#### **VIII. Hospitalization.**

- A. Extend usual hospital stay as indicated.



## REPORT ON THE TENTH NATIONAL CONFERENCE ON PHYSICIANS AND SCHOOLS

It was a privilege to have represented the Connecticut State Medical Society at the stimulating biennial conference, held in Chicago on September 23-25, 1965, and sponsored by the American Medical Association. An opportunity was provided for communication and discussion with members of several professions involved in School Health.

The plan of the conference put emphasis on some current problems facing our youth, namely sex education, drug misuse and mental health. It also provided for an evaluation of the recommendations of past conferences.

The excellent guest speaker presentations were informative and served to initiate discussions. Some salient remarks follow. It was stated that adaptation to stress often leads to better function. Young people should, therefore, be helped to understand that stress and adversity is a meaningful part of their development. Stress adaptation is believed to be one of the several factors which influence youth in solving personal difficulties or in coping with world problems. It was also suggested that youth should be prepared to be "tough minded" individuals, but "tender hearted" (i.e. considerate of others) and dedicated to a higher purpose.

One session considered the opportunities of the school and community in regard to sex education, i.e. the biological aspects as well as the sociological phase (the sex role, family living, etc.). Part of the problem in this matter was felt to be due to parents' inability to discuss the subject plainly and naturally, probably because of a lack of information and vocabulary. Several speakers felt that the schools could remedy this situation with the dissemination of accurate health information and encourage critical thinking for decision in this area. Sound values with respect to sex roles, boy-

girl relationships, preparation for marriage and family living could thereby be developed.

Also, the increasing experimentation and curiosity of young people with harmful substances, narcotics and "soft drugs" and the availability of these items, makes improved health instruction and education in schools a necessity. This would insure a more effective dissemination of adequate knowledge and the potential dangers of these substances.

Many mental health difficulties are believed to be transmitted by learning processes. Here again, educational programs in schools would reach most children at a time when they are still capable of change, thus aiding, in the prevention of this illness.

To insure that health education programs are not merely health information programs, a recent study project has suggested that the Health Education curriculum be a continuing one and that its development might be based on three major concepts. These are: 1. Growing and developing; 2. Decision making; 3. Interaction. They would provide for a flexibility in curriculum planning and could be used at various grade levels and anywhere in the nation, incorporating the necessary health facts.

The implementation of good Health Education programs in schools has many road blocks, primarily apathy, lack of leadership, individual and community attitudes, lack of statistical data and manpower. It was suggested that Medical Societies could make important contributions in overcoming some of these issues.

Respectfully submitted,

Joseph J. Bellizzi, M.D.

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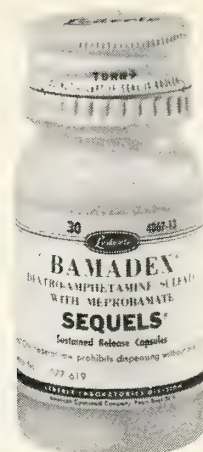
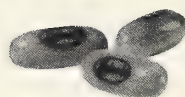
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**Children:** 3 to 6 months — 3 mg. ( $\frac{1}{2}$  tsp.\* t.i.d.)  
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\*Based on 4 cc. per teaspoonful.

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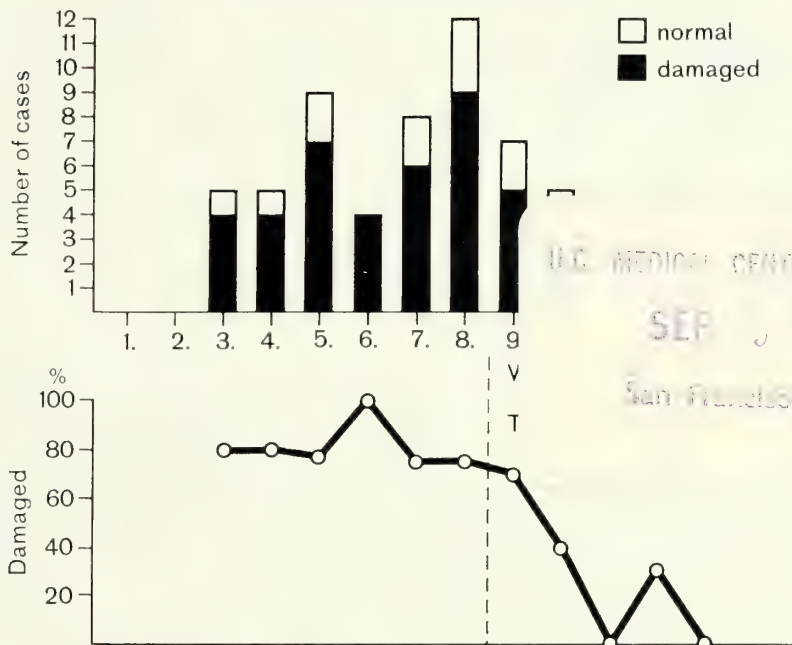


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Connecticut State  
Medical Journal

Vol. 30 / August, 1966 / Number 8

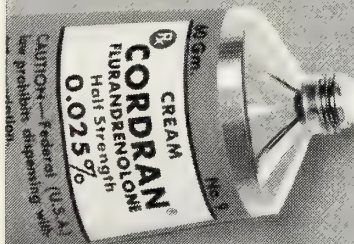
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From Prof. G. Töndury, *Triangle*, Vol. 7, Number 3, Pg. 93, 1965

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# Connecticut Medicine

## editorials

### Etiologic Factors In Human Malformations

Töndury<sup>1</sup> points out that a large undetected percentage of malformed embryos die while in utero and are prematurely expelled. Other embryos are carried to term but are not viable organisms and that the incidence of non-viable organisms is 1-1.5 per cent. However, in proportion to all infants born after the 28th week of gestation and observed for a period of a year after birth, the proportion of malformations rises to 4-5 per cent. In addition the malformations which do not become manifest until later during infancy, adolescence, or in adult life, mount up to 5-6 per cent. Clearly we have here a major clinical problem.

Over the last twenty-five years we have learned that environmental teratogenic factors play a much greater part in the development of human malformations than was often assumed in the past. Neel has made use of voluminous case material at his disposal and found that 20 per cent of malformations were caused by hereditary factors, 10 per cent by chromosomal aberrations, 10 per cent by virus action and in the remaining 60 per cent the cause could not be determined.

If mouse embryos are irradiated beginning in the first half day and on to 14.5 days, it is possible to study malformations in the prenatal and neonatal period and the principle emerges that the type of malformation depends on the stage of development of organs at the moment of radiation exposure. Other factors such as viruses come into operation when the affected organ rudiments reach the phase of maximum sensitivity. Chemical substances however probably act more or less selectively on organ rudiments that are hypersensitive.<sup>2</sup>

In a given stage a substance may produce an effect on the development of the tail bud, another on the formation of cartilage, another on the de-

velopment of the anterior body wall and a fourth on that of the extremities. For the physician, a knowledge of the most sensitive phases to injurious agents in embryonic development is of considerable practical importance. The majority of malformations in man arise as the result of damage suffered by the embryo between the 20th and 40th day. This can be illustrated by several examples given by Töndury.

Hare-lip is connected with impaired development of the nostrils. The olfactory placodes appear in the embryo after 27 days and transformation into nostrils starts at 30 days and is complete after 42 days. If a child is born with a hare-lip it is obvious that the damage must have occurred before the 30th day.

The extremities begin to develop at approximately 26 days. If the child is born without extremities, then the damaging factor was at work prior to 26 days. After this less pronounced malformations such as phocomelia will appear and if the injurious agent began to operate after 29 days only slight distal damage will appear.

Heart malformations with impairment of the septum formation of the originally undivided heart tube only appears if the embryo was damaged prior to the 32nd day, since on this day the septum primum appears, on the 33rd day the rudiments of the interventricular septum and on the 35th day, the septum secundum appears.

The human embryo is very sensitive to ionizing radiation, to radioisotopes, to radio-mimetic substances such as aminopterin and others which are cytotoxins used for the treatment of leukemia. All these will damage the proliferating blastema and organs. Clearly irradiation to the pelvis must be avoided in pregnancy. Furthermore, aminopterin can kill the embryo and in the critical phase of pregnancy act as an abortifacient. Estradiol also is teratogenic and attacks the cells of the neural tube

#### THE COVER

Figure 4. Survey of macroscopically and histologically studied human embryos, the mothers of which suffered from rubella in early pregnancy (weekly distribution).

and the blastema of the extremities and surviving embryos are microcephalic, have small eyes and crippled limbs. Thalidomide, tetracycline and other as yet unknown agents can also be teratogenic. Obviously during pregnancy mothers are better off if they can avoid any drug since teratogenic actions of all drugs have not as yet been clarified.

When McAlister Gregg discovered the teratogenic action of the rubella virus on the human embryo, this called attention to the importance of external factors. And when it became possible to identify viruses in embryonic tissue this question was definitely settled. The figure on the front cover shows that mothers became ill without exception in the first trimester of pregnancy and the particular sensitivity of the embryo in the first 8-9 weeks. At least 50 per cent of the embryos exhibited extensive myocardial necrosis terminating further development. If the embryos are less severely damaged then atrial septal defects appear. The most frequently encountered malformations was damage to the crystalline lens. The younger the embryo was at the moment of virus invasion, the more extensive was the cell necrosis.

Similar experiences occurred in fetuses of mothers who had influenza type infection. The young embryos had completely intact but still only slightly differentiated respiratory tracts. But if infection occurred in the late stages of fetal development, the invading virus produced massive lung damage. Although the mother weathers the infection easily, the fetus has no such immunity and its tissues become severely damaged by the invading virus which has passed through the placental circulation. The same findings occurred in chicks when they were vaccinated with virus at various stages of development.

What about other viruses? Töndury found fetuses of three months severely damaged in mothers who had contracted poliomyelitis 4-5 weeks before. In the immature cerebral hemisphere he found numerous hemorrhages. If the fetus was largely mature, then the motor cells of the anterior horn of the spinal cord showed changes similar to that found in a person infected with polio virus.

In theory then it may be assumed that any virus can be teratogenic if it invades also the fetus at a sensitive point in its development. For example, Töndury found crystalline lens damage in embryos whose mothers had mumps or hepatitis. In mothers who had been revaccinated with vaccine virus, he also found two embryos expelled spontaneously who exhibited vaccinia with damage to the epidermis and to the mucous membrane of the foregut as well as damage in the placenta itself. But there were no malformations as in the case with rubella virus.

The information presented by Töndury is a warning against vaccination with any live virus at any time throughout the whole period of pregnancy, against irradiation of the pelvis, against taking any drugs during pregnancy known or not known to be teratogenic unless absolutely essential to preserve the mother's life. It is a warning against atomic radiation and a plea for vaccinating women with vaccinia, rubella, polio and even influenza if possible before pregnancy is undertaken, in order to reduce incidence of fetal injury and death.

L.H.N.

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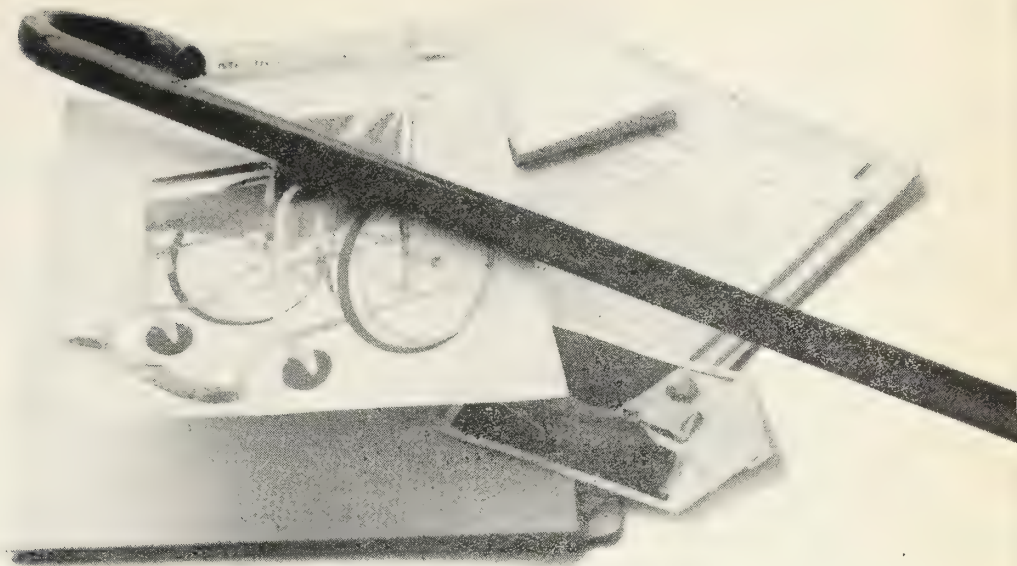
## Toxemia Of Pregnancy

Toxemia of pregnancy is a disease syndrome easily recognized from its three characteristic signs; excessive weight gain, elevation of arterial pressure, and proteinuria, signs that may develop in any order. If more than five pounds weight gain occurs in a week, it is "significant" edema, especially if there is also obvious swelling of the legs, hands, face, and periorbital regions. Elevated blood pressure has to be defined as a systolic of 140 mmHg or over and a diastolic over 90 and this must be higher than normal and maintained for at least six weeks. Proteinuria is the most reliable of the three factors and of course this requires that urinary tract infection must also be ruled out.

There are three categories of toxemia, the acute, chronic hypertensive vascular disease with superimposition of toxemia, and those toxemias related to such other conditions as renal disease, diabetes mellitus, vascular anomalies, endocrine disorders, blood dyscrasias. It is the stage in toxemia when convulsions develop that is termed eclampsia and if the toxemia is allowed to reach this serious stage, then it has a far more serious prognosis for both baby and mother. It is for this reason that instructions such as appeared on pages 525-526 of the July issue should be given to prospective mothers by private physicians and clinics.

At least two things are obvious when one considers the triad of signs in toxemia. One is the generalized vascular nature of the disease. The other is the invariable renal component. This latter is emphasized by the increased frequency of toxemia in patients already suffering from renal disease. The generalized vascular involvement in toxemia, makes it understandable why patients who already have vascular disease such as hypertension, diabetes mellitus or from whatever cause, also have





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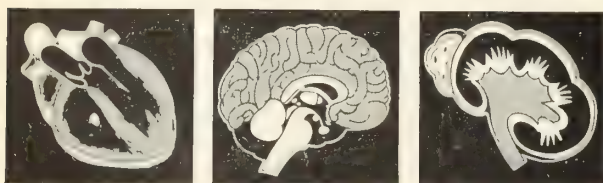


628-6-3614

# Behind continued high blood pressure readings lies the possibility of organic damage<sup>1-13</sup>

**M**ANY OF THE aspects of essential hypertension are unpredictable—either because there are a number of mechanisms involved or because individuals differ in their responses to these mechanisms.<sup>1</sup>

There is one aspect of hypertension, however, that seems, in many cases, predictable. "... when the blood pressure is elevated to a marked degree for an adequate period of time, this in itself leads to perpetuation of the syndrome with resulting vascular damage throughout the body."<sup>14</sup> All too often the disease progresses until there is damage to one of three vital organs: the heart, the kidney, the brain.



"Hypertension is certainly a major factor in the genesis of coronary heart disease, and it is even more important when compounded with obesity."<sup>4</sup>

"[Vascular deterioration] can be clearly seen in the kidney with a degree of damage that can be measured by renal function studies."<sup>10</sup>

"... most evidence suggests that reduction of blood pressure, when it is too high, not only relieves the heart of excess work but reduces vascular damage."<sup>1</sup>

"In short, treatment is indicated."<sup>1</sup>

Antihypertensive therapy will not restore the blood vessels to normal. Yet many of the vascular changes and symptoms caused by increased blood pressure may be arrested or alleviated when the blood pressure is reduced to normotensive levels.<sup>7</sup>

Reducing the blood pressure helps curtail further vascular damage and improves the prognosis — when damage is not too far advanced before therapy is started.<sup>14</sup> Essential hypertension is an indication not only for treatment, but for early and adequate treatment of the patient in question.

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**Contraindications:** Severe renal impairment or previous hypersensitivity. **Warning:** Ulcerative small bowel lesions have occurred with potassium-containing thiazide preparations or with enteric-coated potassium salts supplementally. Stop medication if abdominal pain, distension, nausea, vomiting or G.I. bleeding occur.

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increased frequency of toxemia. Prudence therefore demands that pregnant women in these two categories, be especially carefully watched for the onset of the first signs of toxemia.

Since toxemia of pregnancy is obviously a vascular disease, it is to be expected that its etiology would be found in the existence of a pressor agent and/or an associated acute damage to the kidneys. Following such reasoning further, one would expect some permanent damage in a goodly proportion of such patients months or years after the first insult. Furthermore, recurrent pregnancies in women who had recovered from toxemia should expose the previous insult to the vascular system by making the incidence of recurring toxemia higher than in the normal woman.

It is interesting that in areas of the world like the Northern Japanese Islands<sup>1</sup> where the salt intake is high and so is hypertension, that there is really a high incidence of toxemia in the summer months.<sup>2</sup> The kidney has long been implicated because of proteinuria. For example Altchek<sup>3</sup> found edema of the glomerular endothelium by studying renal biopsies in women with toxemia with the aid of the electron microscope.<sup>1</sup> However, Landsman and Sproul doubt if this is the primary cause. The adrenal gland also has been studied extensively, but although aldosterone excretion is accelerated in toxemia, this is considered to be a secondary finding to probable increased renin liberation by the kidney. However, the edema in toxemia could well be due to aldosterone excessive secretion.

The possibility of a toxin or a pressor material arising from the placenta and its associated structures has been considered by many investigators. Thus Hunter and Landsman<sup>4</sup> have found a pressor polypeptide in the aminotic fluid which they termed Hysterotonin. But what this means has not as yet been completely defined. Another suggestion is that a protein such as renin may be released into the aminotic fluid which in turn interacts with aminotic fluid globulins to produce a pressor polypeptide which may produce the vascular toxic process throughout the body in the kidney, heart, retina, placental vascular bed and elsewhere. This idea is, of course, an analogy of the well-known mechanism of renin-angiotensin and secondary aldosterone mechanism in renal disease. It is clear that we may be approaching the cause of toxemia of pregnancy, but much more needs to be done before its etiology is finally established.

As was mentioned above, if the underlying disease in toxemia is an acute generalized vascular disease then it should leave a permanent mark upon the vascular system in a goodly proportion of women who have recovered from toxemia. Such

women should show a significant increase in incidence of permanent hypertension. Furthermore, recurrence of toxemia in subsequent pregnancies should increase in incidence. An attempt to determine the validity of such inferences was undertaken by Smythe, Dennis, and McIver<sup>5</sup> in a 4½ year prospective study of 158 patients, 86 of whom had pre-eclampsia, 25 eclampsia, six hypertensive cardiovascular disease and 43 normal controls.

The study reemphasizes that with the passage of every year, toxemia of pregnancy plays an important role in the genesis and advance of degenerative vascular disease. In half of the pre-eclamptics, hypertension reappeared with subsequent pregnancies and one-fifth have become permanent hypertensives. The true eclamptics had even a higher incidence of recurring hypertension. None of the 34 controls developed hypertension.

These clinical findings are consistent with those obtained in the 118 renal biopsies taken by these authors six months to 4 years after the initial episode of toxemia in 61 of these patients. Arteriolar lesions persisted in 47 per cent of the biopsies at six months and in 20 per cent of those at 1-4 years. This is exactly the percent age of recurrences of toxemia in subsequent pregnancies and development of permanent hypertension.

Despite the usual opinion that glomerular and arterial lesions of pre-eclamptic toxemia heal or disappear, the true fact is that the vascular insult of the first episode of pre-eclampsia is not completely reversible in almost half of such patients and sets the stage for recurrences of toxemia in subsequent pregnancies. Pre-eclamptic toxemia is clearly an important event in the natural history of arteriolar vascular disease in women. It is obvious why a pregnant woman should be carefully watched for the triad of signs that herald the onset of toxemia, especially in one who has had toxemia or has hypertension and/or vascular disease. It is ample justification for the instructions to the pregnant women found elsewhere in this issue.

L.H.N.

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## Compensation For Heart Attacks Occurring During Work

The "Report of the Committee on the Effect of Strain and Trauma on the Heart and Great Vessels" of the American Heart Association published in 1962 and dealt with in these pages<sup>1</sup> is not lengthy and displays an unusual amount of wisdom because the committee also included a legal subcommittee whose report is very informative. The whole committee report revealed the practical problems, reflected an interdisciplinary understanding and clearly established that the members had a faculty of clear thinking based upon much practical experience. The first of the specific recommendations is "that further consideration be given to the possibility of removing heart disease from the provisions of the Workman Compensation Acts and handling it under various insurance coverage."

It might be interesting to consider why this should be so. The first is what might be called the Doctor's Dilemma. The physician of such a cardiac patient properly abhors the part he needs to play in the courts of law. Here he may be forced into an adversary approach. His concept of causality is not that of "sequence" which many courts and lawyers still pursue, but "consequence," the only scientific basis for etiology. The doctor is subjected also to the tedium of waiting for the trial and the gamesmanship within it. But perhaps from the physician's point of view most important is the threat of a rupture of the physician-patient relationship, if in his wisdom he concludes that no relation existed between a patient's work and the heart attack.

Most physicians it must be said do find it difficult to treat a patient and assist in his recovery without becoming emotionally invested in him and his welfare generally. For this reason it becomes difficult for the claimant's physician to be an objective judge of the possible relation of an incident at work to a subsequent heart attack, especially when medical knowledge about such a relationship until a decade ago was inadequate and in some instances is still inadequate. Furthermore an adverse recommendation by the doctor may prevent receipt of financial aid to which the patient and his family believe they are entitled and which they often need badly. Indeed if the patient is aware that a negative opinion by his doctor prevented such an award, it inevitably destroys the patient-doctor relationship. It really would be better that the attending physician, even if a specialist should not be asked to make a judgment as to causal relationship on his own patient and as is done in Washington State, have an impartial panel to whom the claimant may be referred to make this judgment.

It is all too easy for the claimant or even his physician to associate two events closely related in time as a cause and effect relationship. As noted above sequence is not consequence and yet it is likely that such a mental confusion is operative in many cardiac industrial cases. Cases still appear in which the physician states in essence "the heart attack happened on the job, so the job must have caused it." This is no different than saying the heart attack happened while he was asleep, therefore sleep must have caused it.

Clearly this is unsound reasoning even if it is embellished somewhat by introducing elements of emotion or nervousness (never stating how intense and for how long). The inevitable consequence of this type of reasoning is to raise the cost of maintaining an adequate insurance program for injuries clearly related to work, and it also discourages employers from hiring cardiac workers or permitting cardiac patients to return to work for fear of increasing insurance costs.

However, as long as compensation laws are in existence in many states, the need for establishing a relationship between an industrial effort and a heart attack exists and it was necessary to establish medical criteria to guide in this determination in any individual case and this is what the report of the Committee of the American Heart Association was all about. In Washington State<sup>2</sup> they established not only these criteria but they set up a cardiologist panel to guide the Commission in their decisions. Two things promptly happened; there was a decline of awards from a total of 124 in 1950 to average 55 since 1955 when the criteria and cardiologist panel came into being. Furthermore the incidence of disagreement among doctors fell from 24 before 1955 to 12 after 1955. This data suggests that the introduction of the criteria and panels was of value particularly in achieving a decrease in inconsistent medical opinions and a decrease in the number of appeals. The cases were settled more equitably with greater speed and less litigation. Processing of the remaining cases led to more rapid settlement, earlier availability of benefits, and earlier return to work or all three.

In the great majority of cases Board decisions were made consistent with the medical judgment received. In most cases there was agreement among informed physicians. There were some differences of medical opinion on the basis of available medical information which could be supplemented in part by investigation by an adjuster who is told by the physician the missing facts needed for an informed opinion, and especially by post-mortem findings. At the end of this column will be found the criteria used by the Washington Department of Labor and Industries and written by a commit-



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tee of the Washington State Heart Association. It is not significantly different from that of the American Heart Association criteria.

In the meanwhile we must remember that reducing the number of grants for compensation of heart diseases occurring during work has also increased the number of sick workers who are denied compensation. Would it not be preferred that social and medical security in general apply to the worker whether at work or not in regard to cardiac death or disability? Meyer Texon<sup>3</sup> in 1954 stated "Just as the question of fault for injury was eliminated by the Workman's Compensation Law so all questions of time, place, and causal relation could be eliminated by a comprehensive accident and sickness disability benefit law."

The present arrangements may "discourage physical activity. It will encourage exhibition of undesirable traits of character (as the concealing of symptoms outside work, and lack of self-control at work), and inculcate among medical referees an unconscious self-deception practiced under the cloak of social justice."<sup>4</sup> It is time we re-evaluated our thinking about compensation for heart attacks occurring during work. The sick worker needs help whether the illness was caused by his work or just happened in the course of his work.

*Criteria of the Washington State Heart Association used to establish a causal relationship between work and heart attacks.*

- a. Sudden death from acute coronary disease in which symptoms developed during the course of or immediately following an exertion or strain that is both excessive and unusual for the particular individual concerned; this exertion may be either physical or emotional. Stated conversely, any such exertion or strain which is usual for the individual concerned should not be considered a cause of acute coronary disease.
- b. Coronary occlusion with myocardial infarction when the first symptoms or signs occur during or immediately following an exertion or strain of the type described in (a).
- c. Acute coronary insufficiency when the symptoms or signs appear for the first time during or immediately following an exertion or strain of the type described in (a).
- d. Acute pulmonary edema or heart failure first occurring during or immediately following an exertion or strain of the type described in (a).
- e. Contusion of the Heart when symptoms or signs occur within a reasonable time after non-penetrating injury to the chest.
- f. Serious cardiac arrhythmia occurring during or immediately after chest injuries or exertion of the type described in (a).

L.H.N.

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## Kinekard: An Exercise In The Scientific Method

Recently a group of workers at the Baker Medical Research Institute in Melbourne, Australia, have isolated from the blood plasma of many species of animals a substance which has a powerful action on both heart and blood vessels, which has no species specificity and which they called Kinekard.<sup>1</sup>

There are a number of cardioactive substances in plasma which was recognized as long ago as Bowditch's time in 1872. When a hypodynamic state was induced in a toad heart by prolonged perfusion with a protein free salt solution, it could be reversed by substituting serum for the perfusion fluid. Certain simple experiments could be done on the toad heart to determine whether the substance resembles a cardiac glycoside. Nayler and McCulloch<sup>1</sup> found that it does not because it acts promptly whereas glycosides take up to an hour before its action develops.

Another problem opened up by this observation on cardioactive action of plasma is whether the plasma contains a factor which regulates the calcium binding capacity of the cell membrane and so to some extent regulates contractility of the myocardium. This question is not yet answered although Hadju and Leonard<sup>2</sup> have described just such a substance, cardioglobulin, a plasma protein which increases contractility of isolated cardiac muscle.

Nayler and McCulloch<sup>1</sup> also observed seasonal variations in the plasma cardiotoxic activity of the toad and this raised the possibility that plasma normally contains a substance which may be under hormonal control. In a hibernating toad when they administered anterior pituitary extract, it partially restored the cardiotoxic response to plasma in the winter toad. Thus it became apparent that the cardioactive substance in plasma may be under hormonal control.

This problem could not be pursued further until Curtin and Nayler<sup>3</sup> in 1963 succeeded in isolating from human blood plasma the specific plasma frac-



tion that exercises a positive inotropic action on the isolated toad heart. The substance turned out to be a polypeptide with a molecular weight of 5000-8000 which they chose to call kinecard. In amphibian plasma kinecard activity was low during hibernation but can be increased by injecting anterior pituitary extract 48 hours before assay as noted above. Adding kinecard to the perfusion fluid of an isolated toad heart preparation produces an increase in force of contraction, augmentation of oxidative metabolism, increase efficiency of energy conversion and a greatly reduced response to cardiac glycosides. This one would expect if the inotropic action of kinecard augmented contractility maximally. This same response the authors found in many small mammals as well. Protease completely destroys the action of kinecard, proving that it is a polypeptide.

With present methods of extraction, approximately 60  $\mu\text{g}$  can be recovered from one liter of human plasma. Its inotropic action is 10 times greater than that produced by nor-epinephrine. If injected intravenously into an anesthetized rabbit in a dose of .025 to .05  $\mu\text{g}$  per kg there results a marked pressor response. If this were due to liberation of nor-epinephrine then it should be abolished by agents like reserpine which depletes nor-epinephrine states or by prior administration of pronethalol. The kinecard action was not affected and the conclusion must be that B adrenergic neurohumors are not involved in kinecard's pressor response and immediate increase in cardiac output. Neither is the response modified by prior removal of kidneys or adrenals and this rules out epinephrin and the renin-angiotensin and aldosterone system.

There is a pressor response to kinecard which is due to a direct action on blood vessels. This is proven by experiments on dogs with a cardiopulmonary by-pass and in various hind limb preparations. The pressor response is not uniform throughout the vascular system because it is accompanied by a redistribution of blood flow in various regions, there being a decrease in the hind limb and renal vascular beds with a concomitant increase in coronary blood flow. Coronary artery dilatation is produced whether the heart is or is not artificially paced or is performing useful work. This action strongly resembles that obtained with alpha adrenergic discharge and epinephrine and in fact agents which antagonize epinephrine effects, like phenoxybenzamine also completely abolish kinecard action on the vascular system.

If kinecard has an epinephrine like action, then it should increase contractility of vascular muscle and induce relaxation and cessation of contraction in non-vascular muscle. This in fact is reported by

Lowe and Nayler.<sup>4-5</sup> Aortic strips suspended under isometric conditions contract with kinecard and this action is blocked by phenoxybenzamine. Similarly kinecard caused relaxation and cessation of spontaneous contractions of an isolated segment of rabbit ilium. It also inhibited spontaneous contractions as well as acetyl-choline induced contractions in an isolated uterine segment.

Kinecard concentrations in the blood as mentioned above are somehow dependent upon the hypothalamic pituitary region. In the hibernating toad kinecard activity is very low but can be restored to normal by parenteral injections of anterior pituitary extract 48 hours before measurement. In the same way kinecard levels of plasma go down if one produces surgical damage to the hypothalamic pituitary region. Clearly in some way as yet not worked out, this region of the central nervous system is involved in the control of circulating kinecard.

It will be noted that there are many similarities and also differences from various other substances in plasma which act on the vascular system. Catechol-amines, and other polypeptides have entirely different molecular weights than kinecard. However, it certainly seems likely that its pressor activity is mediated through alpha adrenergic receptors, though not by release of locally stored catecholamines, since it acts even in absence of stored catecholamines and in the absence of the adrenals.<sup>6</sup> Its inotropic activity in the isolated heart and its pressor activity sets it apart from bradykinin. Its ability to increase coronary blood flow is in sharp contrast to action of oxytocin and vasopressin which sharply reduce coronary flow.

Thus it appears after beautiful biochemical techniques that isolated kinecard in pure form and after extensive pharmacologic investigations to pinpoint the nature and site of action, that kinecard is a previously unknown highly potent stable plasma constituent that may be a component of the mechanism which regulates the cardiovascular system. The widespread occurrence in all animals studied and lack of species specificity suggest that it should have biologic significance. The fact that it occurs in relatively equal amounts in normal and heart failure patients reduces our enthusiasm that we may have in kinecard a breakthrough in treating the failing heart.

L.H.N.

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## Aerobic Capacity In The Cardiac Patient

We have long recognized that patients suffering from inflammatory diseases of the heart need rest. We are coming to accept as a fact what was in doubt two decades ago that patients with ischemic conditions of the heart do not need rest but graded degrees of exercise. Exercise in athletes may lead to cardiac hypertrophy and presumably increased coronary circulation. The presumption therefore is that exercise might also benefit the coronary circulation when it has been impaired by degenerative disease. If so how much should be prescribed—Telling a patient to “take it easy,” “don’t do too much,” is more likely to be anxiety provoking than therapeutically beneficial. We should be able to tell our patient specifically when he is doing enough and when he is doing too much exercise.

To give sound advice to our patients, however, requires our understanding of certain concepts relating to exercise. One is the patient’s “aerobic capacity” and how he can recognize it. This concept is based upon the maximum amount of oxygen that any person uses at maximum levels of exercise. A fit young person utilizes 3.5 to 4 liters of oxygen at his maximum capacity. However at this level there accumulates a large oxygen debt, a build up of lactic acid in the blood, a rising pulse rate and body temperature and rapid onset of fatigue which soon limits the exercise. At half maximum levels of exercise none of these signs are observed because the subject now is operating within his “aerobic capacity.” He is not producing an oxygen debt.

For example, a given normal middle-aged person can walk four miles an hour, use up  $O_2$  at the rate of 1.1 liters per minute and his pulse remains steady at 120.<sup>1</sup> At this rate he can continue to walk for 10 miles and when he stops, the pulse returns to the resting level within five minutes. This means

the oxygen debt is very small, the blood lactic acid does not change and no fatigue develops. However, if he walks 5 m.p.h. using 1.5 liters  $O_2$  per minute, the pulse will not remain steady at 120 but continue to rise slowly. Fatigue sets in because his muscles accumulate lactic acid, his respiration increases and he would have difficulty in continuing after about one-half hour. In other words, this person has exceeded his aerobic capacity which was 1.1 liter of  $O_2$  per minute.

We must recognize then, the symptoms that develop when any person exceeds his aerobic capacity; tachycardia, dyspnoea, fatigue, and of course in some forms of ischemic heart disease, anginal pain. Each person’s aerobic capacity varies and is limited by the power of the circulation to transport  $O_2$  to the working muscles and to his heart muscle. However, there seems to be no reason why such a patient should not work up to the limit of his aerobic capacity but, of course, not beyond it. Such exercise in fact could be beneficial.<sup>2</sup>

It stands to reason that for physiological studies of maximum exercise capacity and aerobic capacity a power-driven treadmill which would allow for accurate grading of exercise and measurement of oxygen consumption would be necessary. Such information in fact is the foundation for the concept of aerobic capacity and the reasons for the symptoms that develop when this limit is exceeded. But the physician cannot accompany his patient through every stage of activity and the differing intensities with which they might be carried out. He does, however, have clues as to the symptoms and signs which develop in the form of tachycardia, dyspnoea and fatigue in a patient who exceeds his oxygen capacity.

We might ask ourselves as to what sort of exercises are likely to be within the aerobic capacity of patients. Walking is an activity which can be readily graded to suit a patient’s oxygen capacity. The energy required is directly related to speed and to the weight of the subject and is found by Passmore to be the same for both sexes. However, walking up a moderate grade (1 in 20) increases expenditure of energy by about 30 per cent but walking on a steep hill (1 in 10) the energy needs are doubled. Increased weight of obese subjects imposes a handicap and many could not walk at four m.p.h. until the weight has been reduced.

There are many recreations which provide suitable “light” exercise. Industrial work has been classified as light<sup>3</sup> if it requires an expenditure of energy 2.5-5 kilocalories per minute, as moderate if between 5-7.5 kilocalories per minute, and as heavy if over 7.5 K.C.p.m. Recreations can be similarly classified. However, the physician can recognize when his patient exceeds the oxygen capacity



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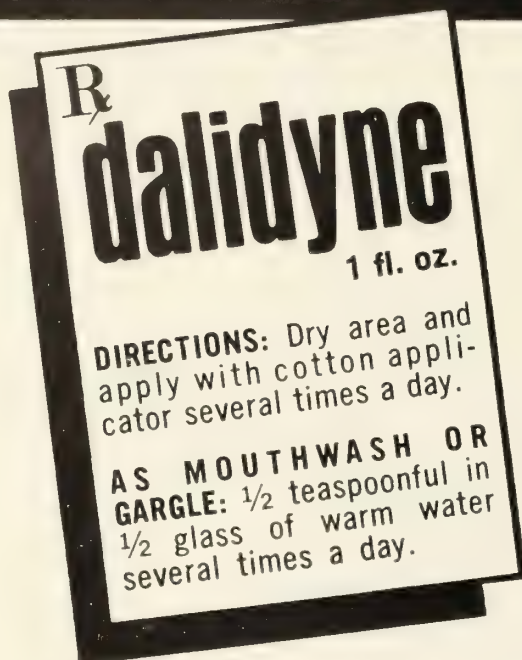
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by inquiring at what point the patient begins to experience tachycardia dyspnoea fatigue and perhaps anginal pain.

Archery, dancing, golf, billiards, fishing, swimming, bowling, gardening, table tennis and croquet were found by Passmore in exact studies of oxygen utilization to provide beneficial and enjoyable exercise for partially incapacitated persons. Of course, we must not forget that many of these recreations can involve heavy exercise at times: the sudden speed-up of dancing, vigorous digging when gardening, use of heavy machinery to do gardening with, can quickly convert light into heavy exercise. If, however, the activity is done slowly and deliberately such exercise as weeding, hoeing, pruning and bedding, can be made into "light" exercise. Golf is usually light exercise but not on a hilly course or a strong wind. One can swim slowly and leisurely, lightly exercising all the muscles of the body since the swimmer is relieved of most of the effort required to support the body weight.

The list of exercises mentioned above is by no means complete, but it does offer a choice of active recreations which may be recommended to middle-aged and elderly patients with and without cardiac weakness provided they always use "moderation." However, as physicians we must not leave them with vague words like moderation. We must explain to them the symptoms which arise when their activity exceeds their oxygen capacity. These guide-lines will help them to sense the symptoms which arise when they are exceeding their oxidative capacity and permit them to enjoy recreational activity and all the benefits to be derived from them.

L.H.N.

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## Calcium And The Heart

Muscular contraction has a chemical basis and can be studied in a test-tube, but it required first the discovery of the contractile protein actomyosin, of adenosine triphosphate (ATP) as the energy source of contraction, and the recognition that a portion of the actomyosin supplied the enzymatic activity required for the utilization of ATP.<sup>1</sup> Now, if we add ATP to a protein suspension of actomyosin in the presence of calcium and magnesium, then shortening of actomyosin occurs. An intact resting

cell has all these constituents, but contraction does not occur until the cell is excited by an electrical or nervous stimulus. How then is muscle maintained in a state of rest despite the presence of all the ingredients for contraction? A further question presents itself. How is the change from rest to activity accomplished by excitation.

It has been known since Ringer's time that without calcium cardiac contraction ceases and since Mines classic experiments in 1913 that calcium is needed for cardiac contraction but not for electrical activity of the heart. How then does the calcium work in the excitation contraction coupling? A part of the answer comes from studies on skeletal muscle.<sup>2</sup> The cell itself has a considerable amount of calcium but the ionic calcium in the immediate environment of the contractile protein is extremely low being approximately one-tenth of that required for contractile activity. However there exist all along the contractile protein intracellular organelles called "relaxing factor vesicles" because they sequester calcium.<sup>3</sup>

These vesicles possess a limiting membrane (quite analogous to the cell membrane) across which calcium is actively transported from cell cytoplasm into the interior of the vesicle. In this way the calcium is anatomically very close to the contracting protein but not directly available to it. There obviously must be some mechanism to increase calcium in the cytoplasm surrounding the contractile protein before contraction can occur. One must therefore postulate that local increase in calcium is effected by a sudden release of calcium from the vesicles as a result of excitation and thus permitting contraction to occur. This is then followed by resumption of calcium uptake by the vesicles leading to relaxation.

In the heart cell local increase in the concentration of calcium is also necessary for contraction, but here at least part of the activating calcium ion enters the cardiac cell from the external medium rather than from the intracellular vesicle.<sup>4,5</sup> When we reflect that the extracellular ionic calcium concentration is more than 1,000 times that in the cell interior, one realizes that chemical forces would strongly favor movement of calcium into the cell, unless the cell membrane interposes a resistance thus preventing calcium from diffusing freely. When cardiac muscle is stimulated, only then does the permeability of the cell membrane to calcium increase so that extracellular calcium can diffuse into the muscle. This calcium is essential for contraction in the heart and no contraction occurs in the absence of extracellular ionic calcium. What is especially significant is that the magnitude of the contractile response appears to depend on the amount of calcium which enters during the period

of membrane depolarization. This amount can be increased by increasing the external calcium concentration or when the duration of depolarization is prolonged. Either intervention leads to an increased contractile response.<sup>6</sup>

The return of the resting state after contraction is completed, must be accompanied by the removal of the calcium which had entered the cell. We must postulate therefore that the cell membrane possesses an active transport system which returns the activating calcium back to the extracellular fluid. The heart muscle cell like the skeletal muscle cell also has a vesicle system. Apparently in the heart, the vesicle system is not sufficient for full activation of the contractile protein. An additional influx of extracellular calcium is required and the magnitude of the influx influences the strength of the ensuing contraction. In the dog heart Stanley and Nahum have found that reducing extracellular calcium to one-tenth normal completely abolishes cardiac contraction.

It is apparent that excitation contraction coupling and gradation of contractile response are closely related in cardiac muscle. One would therefore expect to find mechanisms in the intact animal for regulating cardiac contractile force by altering the amount of ionic calcium that enters the cell during activation. Leonard<sup>7</sup> has found a cardioglobulin in the plasma which increases contractility of isolated cardiac muscle. This cardioglobulin is bound to calcium and may release its calcium into the cell. Perhaps this protein is the one which maintains normal cardiac contractility through calcium release at the membrane.

The regulation of contractile response through the amount of calcium entering the heart cell during depolarization could be accomplished in other ways. For example, there could be control of the extent of increase in cell membrane permeability to calcium occurring during excitation. There could be produced great reductions in the extracellular ionic calcium which could abolish contraction. Such a preparation might serve to study energetics of cardiac cells not related to contraction. It might well turn out that certain types of congestive heart failure result from disturbances in control mechanisms that interfere with delivery of calcium during excitation.

Clearly there are many unsolved clinical problems of heart failure. Realizing the importance of the cell membrane and "relaxing factor" vesicles in excitation contraction coupling, we have a new frame of reference for further study which hopefully will yield new contributions to be applied to improve the failing heart.

L.H.N.

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## Curing The Carrier State Of *Salmonella Typhosa*

The only known reservoir of *Salmonella typhosa* is the human patient or carrier. The problem is very considerable since over 2,000 cases of the disease occur annually of whom three per cent are destined to become carriers. Tynes reported that 3,600 chronic carriers of *Salmonella typhosa* were known to health departments of 46 states and the District of Columbia. Without doubt new carriers are added every year.<sup>1</sup>

The eradication of typhoid fever depends, then, on the elimination of typhoid bacilli from their human hosts. We all recognize the hazard posed by salmonella carriers particularly among food handlers. Although the carriers themselves are not ill, eradication of their pathogenic bacilli involves prolonged use of antibiotics and even cholecystectomy. One would suppose such procedures may be resisted by "healthy" people. However, the typhoid carriers once they are discovered feel themselves to be "unclean," pariahs, social outcasts. Their choice of occupation is limited. They become afraid of normal social intercourse. Their families are usually subjected to periodic immunizations with typhoid vaccine, sometimes with unpleasant reactions. In consequence it is not difficult once the carrier is discovered to induce him to undergo treatment for eradication of the pathogenic organism he harbors.

The susceptibility of most strains particularly of *S. typhosa* to many antibiotics including some that are normally classed as bactericidal, suggests that a





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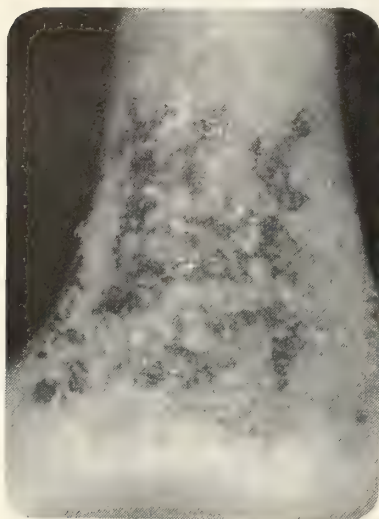
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proper use of these agents alone should offer a solution to the problem of eradicating the carrier state. There is one difficulty, however, and that is that the biliary tract is the major site of these organisms and the choice of drugs or other methods of curing the carrier state must take this into account. Obviously antibiotics must enter the biliary tract in high concentration to be therapeutic.

In 1962 Tynes and Utz<sup>2</sup> studied 27 *Salmonella* carriers whom they treated with a variety of antibiotics alone and cured the carrier state in three out of four patients who did not have gall stones. They used chloramphenicol, tetracycline, ampicillin and a sulpha derivative as well as kenamycin which is not excreted in the bile because it is not absorbed from the gastrointestinal tract. However, if the patients had gall stones then only one out of five were cured by antibiotics alone. If cholecystectomy alone was done and no antibiotics were used, only four out of nine patients were cured. A combination of antibiotics plus cholecystectomy effectively eliminated the carrier state in eleven patients.

The question of course arose as to why the carrier state recurred in those patients with gallstones that were not operated upon. Did reinfection come from infected gallstones? If this were true how explain recurrence of the carrier state after cholecystectomy. Is there an antibiotic which could be effective against the carrier state of *S. typhosa* without cholecystectomy?

Simon and Miller<sup>3</sup> asked themselves these questions and report their results of 15 *S. typhosa* carriers with the use of ampicillin. This antibiotic was introduced in 1961 and had a high activity against gram negative bacilli, yielded a high biliary concentration and was particularly effective against all strains of *typhosa*. Because of its availability, lack of any toxicity more significant than allergic reactions common to all penicillins and its high biliary concentration, its potential usefulness in the treatment of typhoid carriers immediately suggests itself.

These authors used high doses of ampicillin up to four grams per day by mouth over a period of four weeks either continuously or with one week nontreatment after the third week, and succeeded in curing 13 out of 15 chronic carriers and achieved negative stool cultures in them during prolonged followup periods. Eleven of the 15 had documented cholecystitis and five gallstones; nevertheless in only one of these was a failure encountered. They concluded that chronic biliary tract disease or even cholelithiasis or both do not necessarily present insurmountable obstacles to successful treatment.

It should be noted that ampicillin in the doses used by Simon and Miller is not without frequent

side reactions which occurred in ten of the fifteen patients varying from loose stools in eight, skin rashes in six, and in one patient severe urticaria which forced the discontinuance of the drug. From Simon and Miller's study it cannot be claimed that ampicillin can cure every typhoid carrier and clearly there will be failure and the relapse rate is still significant.

In the face of cholelithiasis there are both medical and surgical indications for operation. Furthermore, in such patients relapse may force operation. However effective antimicrobial treatment before, during and after surgery should reduce operative mortality and morbidity and allow for better selection of cases when the carrier state presents the chief or only indication for operation.

One question not answered by Simon and Miller's study is whether the gallstones were sterilized by ampicillin in those patients with gallstones that were cured of the carrier state by ampicillin alone. Tynan thought they were not. There is at present no single test to identify the persistent carrier. However it seems unlikely that organisms inside of gallstones would affect the serologic status of a patient unless or until they could also infect the biliary tract.

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## The Pineal Gland, A Neuro-Endocrine Transducer

Some of the earliest observations on pineal function, Relkin in his excellent review points out, come from clinical cases. Parenchymal pinealomas which were found to be associated with depressed gonadal function and non-parenchymatous lesions that pressed upon and destroyed the gland were found to be associated with precocious puberty. Thus it seemed to early workers that the pineal gland was an endocrine gland, but attempts to relate this gland to a specific endocrine function were inconclusive. There develop calcification in the gland as age progresses but early attempts to relate this event to epilepsy, psychoses, muscular dystrophy, also were unrewarding.

In some animals like fishes, amphibians, and some reptiles, the pineal gland is a photoreceptor organ containing sensory cells resembling retinal cones. In the frog, the cells in the pineal gland, like

those in the eye actually convert certain wave lengths into nervous impulses. In the mammals however, the specific parenchymal cell of the pineal gland the pinealocyte is purely secretory and only liberates its hormone under neural control.

In 1958<sup>2</sup> Lerner, et al. isolated melatonin and showed that it produces a contraction of the pigment granules in melanocytes which results in blanching of the skin. Since then, it has been shown that the precursor of melatonin is serotonin which is more abundant in the pineal gland than in any other tissue. Besides skin blanching, the pineal has been shown also to be able to inhibit aldosterone secretion. Furthermore melatonin can suppress certain serotonin actions such as the motile response of the duodenum.

There seems to be a diurnal variation in enzyme activity in the pineal gland responding to light and darkness, a sort of circadian rhythm. The pineal gland of an animal kept in light synthesizes serotonin. The same gland in an animal kept in darkness contains large amounts of melatonin. Thus the pineal gland turns out to be a biological clock, responding to light and darkness, by synthesizing either serotonin or melatonin. This is a very interesting phenomenon psychogenetically. In fishes and amphibia, the pineal gland responds directly to light rays, whereas in mammals the pineal now is separated from direct light but responds to light now through neural connections with the eye.<sup>1</sup>

The real problem is what does melatonin, the product of the pineocyte do. It is found concentrated in the ovary, in the iris as well as in the pineal gland and is taken up also by the brain, the pituitary gland and the vagina. Melatonin seems to be metabolized rather rapidly since in animals kept in light, the melatonin in the pineal gland decreases and so does its content in peripheral tissues. In such an animal the ovaries hypertrophy and there is a tendency to persistent estrus. This activity is promptly reversed in darkness and by melatonin. These observations point up the importance of the pineal gland in the regulation of photoperiodic influences on the gonads. It is interesting that this observation in basic science, the effect of light on gonadal function has been put to use in animal husbandry since it has been found that hens will lay more eggs if the light is kept on in the hen house.

Recently investigators have demonstrated that a light photo-period facilitates the release of gonadotrophic hormone whereas a dark photo-period encourages their synthesis. There must however be the right balance between light and dark periods for gonadotrophic liberation, for excessive light periods will exhaust the gonadotrophic hormone,

while too long a period of darkness will increase synthesis but not release.

Since common lighting conditions also inhibits nervous discharge of the pineal gland, the question presents itself as to how light influences reach the pineal gland. This problem has been much studied since Cajal's day. Axelrod, Wurtman and Winget<sup>3</sup> have demonstrated that the pineal circadian rhythm for synthesis of melatonin is completely dependent on lighting conditions. The light impinges on the retina from which it somehow gets to the preganglionic sympathetic nerves that terminate in the superior cervical ganglions.<sup>1</sup> From there post-ganglionic fibers ascend to the pineal gland where is released norepinephrine or serotonin. These substances act on the pineal cells to either induce or block melatonin synthesis.

Probably impulses reach the pineal gland not only from the sympathetics. We know that the visual system utilizes limbic pathways to influence neural activities in the septum, hypothalamus and brain stem. The human pineal gland receives fibers from the limbic system.<sup>1</sup> Thus there is reason to believe that light influences pineal secretion by pathways through the limbic system as well as the sympathetics. Otherwise how explain Hoffman and Reiter's<sup>4</sup> observations that olfactory stimuli can interfere with the primary inhibitory effects of an active pineal gland?

One question raised by Relkin<sup>5</sup> is whether the pineal gland is an inhibitory endocrine retarding sexual development during the early years of life by controlling the hypothalamus. In favor of this view is that melatonin inhibits synthesis or release of T.S.H. by the pituitary gland. Another argument in favor of this view is that the pineal gland through melatonin exerts its antigonadotrophic activity directly on the hypothalamus as well as the hypophysis. When melatonin is applied to the hypothalamus directly it induces sleep in cats.<sup>6</sup> The pineal gland can therefore also act as a modulator of the state of wakefulness and sleep. Thus the pineal gland certainly has profound influences on the hypothalamus.

The first clinical association between sexual behavior and the limbic system is Erickson's case<sup>7</sup> of a 55 year old woman in whom erotomania had developed as a consequence of a tumor of the paracentral lobule impinging on the posterior cingulate gyrus. Hypersexuality in monkeys and cats were reported after ablation of portions of the temporal lobe. Electrophysiologic changes in many areas of the limbic system have been found to accompany the hormonal discharge of ovulation. In short, the limbic system is involved in sexual behavior, is known to influence sexual maturation and is implicated also in being a mediator of light impulses



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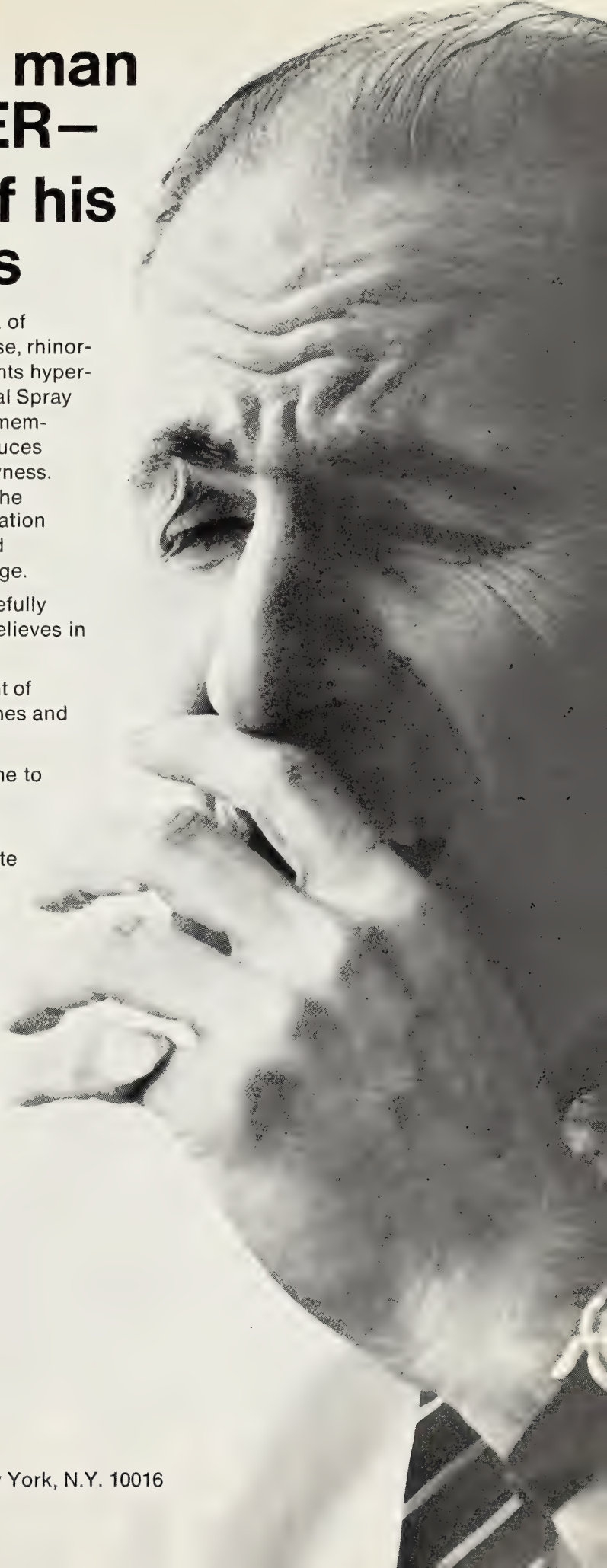
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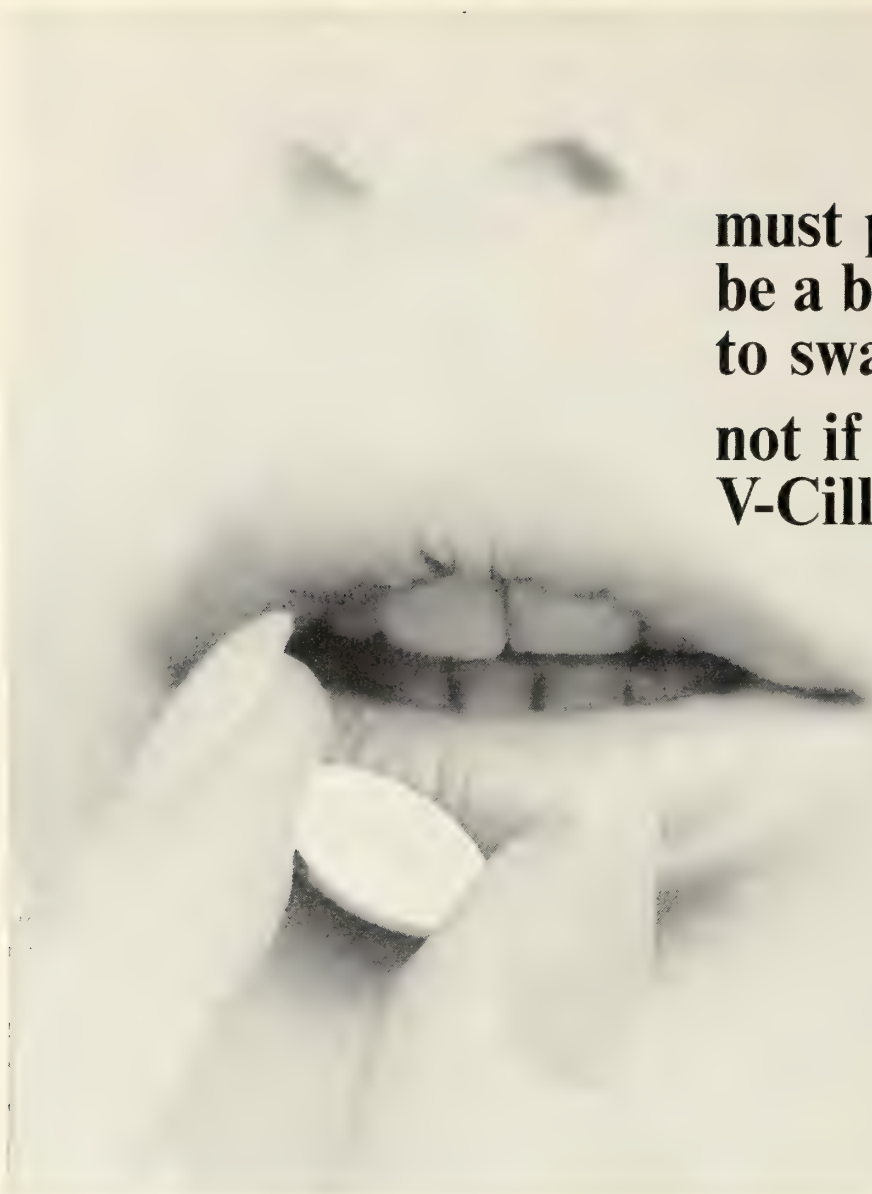
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affecting the septum hypothalamus and upper brain stem. May not the pineal gland be a specialized functional part of the limbic system. For the pineal gland is also known to be a light dependent biologic clock and also exercises control over sexual maturation in mammals via its neurosecretion melatonin.

The pineal gland is therefore a neuroendocrine transducer converting neural into endocrine information. It can be likened to the hypothalamic-posterior pituitary system which secretes antidiuretic hormone and oxytocin. Another neuroendocrine transducing system is the pituitary releasing factors system in the hypothalamus which secretes polypeptides that control the pituitary gland. A fourth such system is the adrenal medulla whose cells respond to nervous input by releasing epinephrine.

L.H.N.

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Hunger And Satiety

Every physician who is engaged in reducing an obese person needs to understand the pattern of hunger and satiety of his patient. It is the modification of hunger and satiety of a patient on a reducing diet which needs to be followed, for this forms the basis of decisions on how allotted calories should be divided among the proper number of meals and snacks. Eventually knowledge of hunger and satiety will determine if an anorexigenic agent is necessary as well as its dosage and timing of administration.

Mayer<sup>1</sup> by a questionnaire given to 800 persons, adult and adolescent, obese and non-obese, attempted to obtain data on the sensory aspects of hunger and satiety in man. They revealed existence of a large number of sensations varying with individuals and in the time in which hunger sensations

are experienced. They originated in the gastric region, throat, mouth, and body. There was great complexity and variability in moods, degrees of urge to eat, and preoccupations with thoughts of food. But in all, hunger was found to be associated with sensations which increase in number and intensity as deprivation progresses.

Satiety on the other hand—the cessation of any urge to eat—is not necessarily associated with any characteristic sensation. Furthermore it does not simply coincide with the disappearance of hunger sensations, but often in adults or others with a change in mood. In children a sensation of gastric fullness accompanies satiety. It would appear that the phenomenon of satiety depends on events occurring at the unconscious level and as a number of neurophysiologic and behavioral animal studies suggest, in the hypothalamus.

Mayer finds that both in obese and non-obese persons abnormalities in satiety might be more prevalent than differences in hunger. Many persons who watch and keep their weight down have learned over the years to eat an amount of food sufficient to allay hunger sensations even though satiety is not reached. These people experience an urge to eat at the end of each meal but the urge is endurable and soon disappears. The so-called re-education of appetite in fact if successful is based on this process. The practical problem of reaching this point where hunger sensations have disappeared even though full satiety has not been reached forms the basis of rational treatment of the obese patient.

Our understanding of the neurophysiologic and biochemical phenomena involved in hunger and satiety is excellently reviewed by Mayer.<sup>1</sup> He points to Brobeck's classical studies on bilateral destruction of the ventromedial nuclei in the rat hypothalamus which caused hyperphagia and obesity. Experiments in the mouse, the goat, and a number of species showed a similar mechanism. However, when more lateral parts of the hypothalamus are destroyed the animals stopped eating completely. These experiments indicate that the ventromedial area of the hypothalamus appear to act as a satiety brake inhibiting the constantly acting lateral "feeding" areas

The question of course arises by what mechanisms these nuclei are set into operation. One idea was that the neurons in the ventromedial area respond to the levels of blood glucose. If the blood sugar is raised by injections of glucagon then gastric contractions cease. This does not happen if the ventromedial nuclei are destroyed. It is clear that the ventromedial area exercises a definite measure of control over gastric hunger secretions and it does this in response to an increase in glucose availability. If one cuts the nerve connections from

the nervous system to the stomach (the vagus) gastric secretion and motion ceases.

By beautiful, highly technical methods Mayer found a greater uptake of glucose in the feeding areas of hungry rats, whereas fed animals showed a relative increase in oxygen and glucose uptake by the ventromedial regions. The conclusion is unmistakable that a glucostatic mechanism appears to be one of essential processes through which the metabolic requirements influence the "feeding" mechanism and through which energetic homeostasis is maintained in all animals.

The hypothalamic factors controlling hunger and satiety are acted upon at a given time to influence food intake by many factors other than the glucostatic mechanism. There appears to be a thermostatic component sensitive to elevation in body temperature which can shut off feeding behavior. Some may respond to high protein intake, gastric distention and dehydration. The monitoring of food intake by the mouth, pharynx, taste, emotion and habit, may at a given moment also influence food intake. Finally, Mayer points out the long term factors such as the state of the adipose tissue which also may regulate food intake.

The servomechanisms whereby the body adjusts ingestion of food to requirements for homeostasis and growth are thus becoming clearer through our recognition of the origins of hunger and satiety and the centers in the hypothalamus which control these sensations. In general, bodies remain remarkably constant in weight. This it does through adjustments of energy intake to expenditure on a day to day basis. There must however be longer term regulation of food intake which corrects the errors of the day to day regulation.

L.H.N.

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## Glucostats In The Body

Glucose is the vital substance which the brain uses for its energy requirements. During diabetes or normal states the brain oxidizes glucose seemingly without the aid of insulin. So dependent is the brain upon glucose that there is a hypoglycemic threshold which when breached leads to convulsions.

Certain special parts of the brain have their own glucostatic mechanism. For example, the ventromedial area of the hypothalamus shuts off the "feeding center" of animals when the blood glucose level exceeds a certain amount. Conversely the "feeding center"—the more lateral areas of the

hypothalamus—lead to sensations of hunger and appetite when the blood glucose level tends to fall below a certain level. This type of glucostatic mechanism in the hypothalamus is obviously an indirect attempt to regulate blood glucose levels by means of the sensations of hunger and satiety.

The beta cells of the pancreas operate in an equally intimate relation to blood glucose levels.<sup>1</sup> As blood glucose rises the beta cells respond by liberating insulin and this servomechanism gets shut off as the blood glucose level falls. In consequence we find that mammals maintain a concentration of glucose in the circulatory blood that varies little with feeding or fasting and this level lies approximately midway between the concentration at which it spills in the urine "the renal threshold" and the concentration at which the brain is just able to extract adequate amounts of glucose to maintain normal function.

The physiologist may well ask what can be the mechanisms by which the beta cell like a continuous auto-analyzer detects glucose concentration and in normal persons responds appropriately. He may ask further whether the beta cell always responds in the same way to the same glucose level or whether there are times that its response is delayed or whether there are other times when the beta cell is over-sensitive, responding to normal or even low levels of blood glucose by increased liberation of insulin.

In idiopathic hypoglycemia of infants and children Rosenbloom and Sherman<sup>2</sup> found impaired glucose tolerance which develops either before or after remission of the hypoglycemia. The families of their ten patients also showed a frequency of diabetes mellitus comparable with that of families having children with clinical diabetes. It would seem that as the idiopathic hypoglycemia continues, the glucose tolerance gradually begins to assume the pattern of a familial diabetic disorder. In short over responsiveness of the beta cells to normal or low blood sugar levels produces spontaneous hypoglycemia in infancy and this may be an inherited disorder of the beta cells which leads to diabetes mellitus later in life.

Slone, et al.<sup>3</sup> studies were undertaken to determine what the insulin blood levels were in infants with idiopathic hypoglycemia. They measured insulin levels in the blood by a radioimmunoassay method, and found a significant elevation of insulin in this rare disease and also wide fluctuations of serum insulin even in fasting conditions in the same patient. Thus the lesions in these infants suffering from idiopathic hypoglycemia appears to be an inability of the beta cell to turn off insulin release when the blood sugar falls to subnormal



levels. In essence, there is an over-sensitive glucostat in the beta cells and as a consequence a mechanism causing excessive work by the beta cells which in time leads to their exhaustion and the onset of diabetes.

There are many conditions that can lead to excessive burdens on the beta cells ultimately leading to their exhaustion and appearance of diabetes mellitus. Growth hormone, excessive adrenal cortical hormone, excessive food intake, and now an over-sensitive beta cell glucostat which under conditions of normal blood sugar levels leads to excessive inappropriate insulin secretion, and ultimately diabetes mellitus. We owe to Rosenbloom and Sherman the recognition that this may be a mechanism responsible for diabetes. In adults also spontaneous hypoglycemia has been found to be an early manifestation of diabetes mellitus perhaps by the same mechanism of excessive burden on the beta cells and their premature exhaustion.<sup>4</sup>

If some beta cells can respond inappropriately to their glucose challenge we are compelled to ask whether other glucostatic mechanisms in the hypothalamus controlling hunger and satiety may also at times act inappropriately and lead to overeating and obesity on the one hand and premature satiety with a resulting excessive underweight on the other. There is much work here that needs to be done since a rational treatment of such cases of obesity can follow only such physiologic information.

L.H.N.

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Immunization Of Infants And Children

The effectiveness of active immunization against diphtheria, pertussis, tetanus, smallpox, poliomyelitis and measles is well established and all children should have the protection of vaccination against these diseases. Immunization with BCG vaccine, however, is advisable only for susceptible children who risk exposure to tuberculosis. A suggested immunization schedule. It was prepared with the aid of Medical Letter pediatric consultants, and agrees

generally with the current recommendations of the Committee on Control of Infectious Diseases of the American Academy of Pediatrics (the Committee is now completing revision of its previous recommendations). Only the recommendations for polio, measles, and tuberculosis immunization require comment.

*Immunization against poliomyelitis.*—Because of ease of administration and the greater duration of immune response, the oral live poliovaccine is favored over the inactivated type for routine immunization in infants. Three doses of the trivalent vaccine (types 1, 2 and 3) are recommended for primary inoculation alternatively, a single dose of each of the three strains may be given separately at intervals of about six weeks. There appears to be no difference in effectiveness, but errors of administration are less likely with the trivalent form. With either, a trivalent booster should be given in one year and again when the child enters school. To minimize the possibility of interference by enteric viruses, oral vaccines are best given during the cooler months.

*Immunization against measles.*—Normal infants should be immunized against measles at nine to 12 months of age. Either live attenuated measles vaccine (Edmonston strain) plus measles immune globulin or, alternatively, further attenuated live vaccine (Schwarz strain) without concomitant immune globulin administration is recommended. (Inactivated measles vaccine should be used when immunization before nine months of age is considered necessary, and in children with debilitating diseases or with a history of convulsive disorders.)

*Immunization against tuberculosis.*—The Academy of Pediatrics advises administration of BCG vaccine in children with negative tests who live in or are going to areas where tuberculosis is prevalent; or who are likely to be exposed to persons with active tuberculosis or tuberculosis arrested less than five years. Where possible, BCG should be given at least two months prior to expected exposure, but it should be withheld where exposure is more imminent.

*Reprinted from The Medical Letter on Drugs and Therapeutics, New York, N. Y., Vol. 8, No. 5, March 11, 1966.*

Note On Cancer Issue

Dr. Henry M. Williams, who was Guest Editor for the June and July issues of *Connecticut Medicine* on cancer, was assisted by the following guest editorial board: Marcus E. Cox, Henry Eisenberg, Robert B. Golbey, Donald P. Shedd, and Carl von Essen.

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# A More Practical And Simplified Method Of Colonic Exfoliative Cytology

## A Preliminary Report

Vincent F. Vacca, M.D. and Vincent A. DeLuca, Jr., M.D.

■ The continuing high incidence of carcinoma of the colon emphasizes the necessity of effective and practical methods of early diagnosis. Exfoliative cytology, of established importance in the diagnosis of cancer in other organs, should be equally as effective when applied to tumors of the colon. Both Raskin<sup>1,2</sup> and Cameron<sup>3</sup> have shown this to be true. However, the complexity of the procedure has kept it from being adopted for general hospital use. As usually carried out, it is a long and tedious procedure, often exhausting to the patient, requiring equipment too complex for use on a large scale, and not of the least importance, is occasionally offensive to the personnel who perform the study.

We have developed a simpler method of performing this procedure which yields readable epithelial cells in high numbers. This method reduces the total time of the procedure, usually eliminates the need for multiple cleansing enemas, and requires the presence of a physician only for the sigmoidoscopic examination. It also includes a simpler method for deriving the cellular material from the enema fluid. This method is presented with the hope that it will be more widely used, resulting in the accumulation of more information concerning colonic cytology in general, with clarification of its true value in the diagnosis of carcinoma and other disease of the colon.

### Procedure

The basic procedure for cleansing the colon used in this study is a modification of that described by Raskin. (Procedure I and II). The patient is prepared with a low residue diet for at least 2 days prior to the study. A laxative is employed in moderately strong doses, given the afternoon and evening before the study. In the majority of our cases, we have used Senokot granules,\* 4 tsp. in water at 1:00 P.M. and 2 tsp. in water at 6:00 p.m. On the morning of the test, the patient is allowed a liquid breakfast.

\* SENOKOT — standardized senna concentrate-Purdue-Frederick Company, Yonkers, New York.

*We are grateful for the support of: The American Cancer Society, Connecticut Division, The Purdue-Frederick Company, Yonkers, New York.*

The procedure is begun with a cleansing enema which, though more conveniently done on a mechanical examining table, can also be done in the patient's hospital bed.

The enema is given with the patient in the Sim's position. The fluid volume used ranges from 1200 to 3500 c.c. of isotonic saline, according to the patient's tolerance. By changing the position of the patient to his back and right side, the entire colon can usually be cleansed.

#### PROCEDURE I

##### A—Preparation

1. Low residue diet for 2 days.
2. Strong laxative day before study.
3. Liquid breakfast day of study.

##### B—Cleansing Enema

1. Sim's position.
2. Enema—1200-3500 cc. saline.
3. Position patient.
4. Evacuate and examine fluid.
5. Rest for 1½-2 hours.

#### PROCEDURE II

##### C—Diagnostic Enema

1. Sigmoidoscopic examination.
2. Insert rubber Ewald tube and withdraw scope.
3. In Sim's position instill 800 cc. isotonic saline.
4. Position patient on back, then right side.
5. Massage abdomen for 5 minutes.
6. Siphon fluid into beaker in ice bath.
7. Remove mucus clumps, smear and fix in 95 per cent alcohol.
8. strain fluid, smear remaining mucus and fix.
9. Centrifuge fluid, smear sediment button and fix.
10. Remove Ewald tube.

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Following evacuation into a bedside commode, the return fluid is then examined to determine the quantity and character of any fecal material present. In a well prepared patient, the fluid itself will have a yellowish tinge and there will be very little powdery sediment at the bottom. One cleansing enema is usually sufficient. However, if there are large fecal particles or gross fecal matter present, a second cleansing enema may be necessary. Rarely, a third enema was used in this series. It has been our experience that a total absence of fecal material is not an absolute prerequisite for a good study.

The patient is then allowed to rest in his own bed for a period of one and a half to two hours. This allows the surface epithelium of the colon to "prepare itself" for exfoliation by loosening its intercellular bonds, a process which occurs naturally, and fortunately for our purposes, occurs much more rapidly in malignant tissues. The patient is then returned to the examining room for the diagnostic enema.

### Diagnostic Enema

This portion of the procedure is begun with a routine sigmoidoscopic examination. Then, with the sigmoidoscope in place, a rubber Ewald tube is inserted through the scope to approximately 35 centimeters, i.e. about 10 cm. beyond the tip of the scope. This insures that the smaller amount of fluid used in the diagnostic enema will pass beyond the natural barrier of the rectosigmoid curve. The sigmoidoscope is then removed leaving the rubber tube in place.

Using the same left sided, head down position as before, 800 cc. of isotonic saline are instilled through the tube. The previous positions of 5 minutes on the back and 10 minutes on the right side are then repeated with the Ewald tube in place. Next, the 4 abdominal quadrants are vigorously massaged for about 5 minutes, with special attention being given to any area containing a suspected lesion. The patient is then placed again on his left side and the fluid is siphoned out through the Ewald tube into a liter beaker  $\frac{2}{3}$  submerged in an ice bath. The fluid will usually gush out in response to the peristaltic contractions of the bowel. Occasionally it will be necessary to help it along with mild air insufflation with a bulb syringe. The fluid thus collected is usually found to contain small fecal particles or powder and often small streaks or clumps of blood and a variable amount of clear or blood streaked mucus clumps.

It is to these mucus clumps that we give our immediate attention. This mucus is removed from the beaker by means of a spatula, forceps, or a bulb pipette. A portion of this mucus is immediately smeared on a frosted glass slide with a spatula,

then thinned out by the "two-slide technique" and quickly placed in 95 per cent alcohol for later staining. The fluid remaining in the beaker is then carefully strained through an ordinary 4 or 5 inch food strainer. Any mucus particles remaining in the mesh of the strainer are also smeared and fixed in alcohol. The filtrate is placed in 60 cc. plastic centrifuge tubes, centrifuged for 2 minutes at 2500 RPM and its button smeared and fixed the same way. Thus we have 3 possible sources of cellular material.

The Ewald tube is then removed and the patient is returned to his bed for a period of rest and observation. If the subject is an out-patient, a period of observation of approximately one hour is wise before allowing the patient to leave the hospital. This will vary, of course, according to the general condition of the patient.

Each part of the procedure usually requires approximately one hour, so that the nurse is with the patient for about 2 hours. The rest period in between and the period of observation following the study do add to the total time for the patient, but we have not found this to be a problem, even with out-patients.

It should be emphasized that once the personnel is trained to do the procedure properly, the physician's presence is required only during the sigmoidoscopic examination.

We have seen that the success of this method is directly proportional to the enthusiasm of the personnel performing the study. It is important to the final results of the study that the nurse is interested enough in this type of work to be willing to face the possibility of an occasional unpleasant and downright messy accident.

We originally trained a Registered Nurse to perform the procedure, and she has since taught other nurses, so that we now have a well trained group, the members of which can replace each other as the need arises.

The RN now makes the mucus smears, thus freeing the cyto-technician from having to be at the bedside during the last part of the procedure.

Two cases are presented to show the value of the method.

### Case No. 1

A fifty-two year old woman was admitted with cramping abdominal pain, associated with nausea and vomiting of one week's duration, and increasing abdominal girth. In 1956, she underwent radical mastectomy followed by bilateral ovariectomy for carcinoma of the breast. During the past year, she had developed progressive constipation, and her abdominal pain actually began approximately one year prior to admission, but was not of concern to her until recently. There had been no melena. She had undergone x-ray therapy for metastatic lesions in the hip.



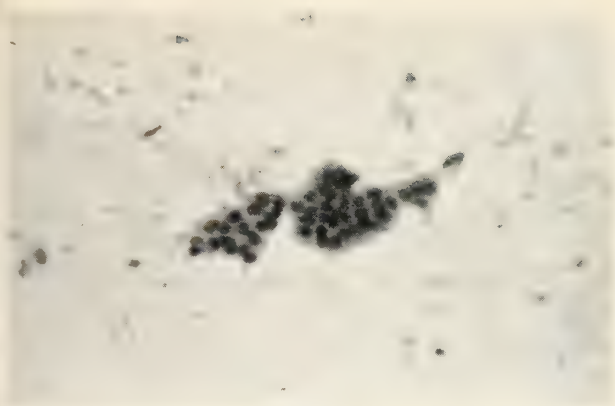


FIGURE I  
Normal colonic epithelial cells.

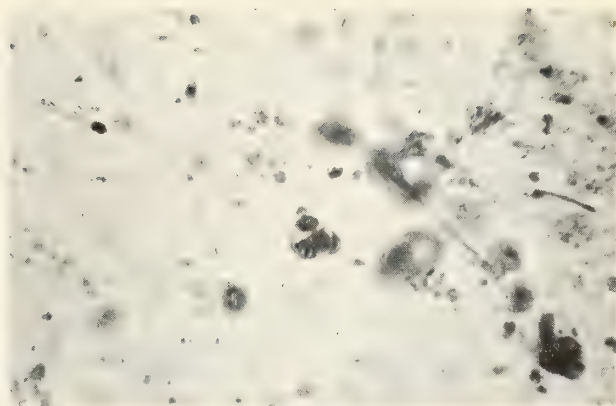


FIGURE II  
Malignant colonic epithelial cells.

Pertinent findings on physical examination revealed the abdomen to be slightly distended, the liver was enlarged and palpable 2 finger-breaths below the right costal margin in the mid clavicular line. Its edge was sharp and smooth. A fluid wave was easily felt. Barium enema examination revealed a narrowed area in the distal transverse colon thought to be due to extrinsic pressure. Cytological studies of the ascitic fluid failed to reveal any evidence of malignancy.

Colonic cytology washings produced normal epithelial cells. Fig. I.

Comment: Fig. I represents an example of typically normal epithelial cells which helped to substantiate the impression that no intrinsic disease existed in the colon.

### Case No. 2

An 80 year old white male was admitted complaining of abdominal pain of 24 hours duration. Over the few months prior to admission, the patient noticed progressive constipation with increasing abdominal distention, anorexia, a ten pound weight loss, and for 24 hours had been unable to pass even gas per rectum.

He was a slightly emaciated elderly man in a poor nutritional state, pale but not dehydrated. His abdomen was distended but soft. Rectal examination revealed no masses, tenderness or blood. Barium enema examination showed an obstruction of the colon at the junction of the descending and sigmoid segments. Colonic cytology washings were positive for malignant cells. (Fig II).

Comment: Fig. II represents an example of typically malignant cells that can be obtained in colonic washings from lesions *above* reach of the sigmoidoscope.

### Discussion

The examination described here may be performed on patients with diverticulosis, diverticulitis,

colonic polyps, unexplained rectal bleeding, change in bowel habits, or suspected colonic cancer. Its place in the study of patients with ulcerative colitis remains to be determined.

Our experience at this time reveals that smearing the mucus clumps simplifies the technique of colonic cytology, and results in adequate numbers of well preserved epithelial cells.

### Summary

In an attempt to simplify the procedure of colonic exfoliative cytology, we have derived a method using the simple smear technique of mucus clumps derived from a saline enema following adequate bowel preparation. It has been our experience that mucus so derived contains adequate numbers of well preserved epithelial cells representative of those lining the colon. The cells found in the mucus are not only greater in number than those derived by other techniques, but are consistently of better quality than those derived from the sediment. The procedure is introduced with the hope that it will be more widely used in other hospitals, leading to a valid assessment of its diagnostic potential.

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# Recent Advances In Leukemia Therapy

Pasquale E. Perillie, M.D. and Stuart C. Finch, M.D.

## Introduction

■ Despite intensive basic and clinical research human leukemia remains a dreaded and incurable disease. Development of definitive therapy has been hampered by a lack of knowledge concerning its etiology. Although there is much to suggest viral transmission, this is far from certain. It now seems likely that leukemia will be neither prevented nor cured until its etiology and pathogenesis are clearly understood. Despite these major obstacles some bold and promising forms of therapy recently have been developed. Some of these new procedures are designed to reduce morbidity but most are directed toward the prolongation of survival.

This report is concerned primarily with a variety of new forms of leukemia chemotherapy and advances in the field of supportive therapy. Most of this information is related to the treatment of acute leukemia but whenever appropriate its application to chronic leukemia will be noted. Conventional forms of leukemia therapy will not be described since they have been adequately reviewed elsewhere.<sup>1-3</sup>

## General Remarks

No discussion of the results of acute leukemia therapy is complete without careful consideration of the characteristics of leukemia. Not infrequently, published reports fail to provide information as to patient age, leukemia type, duration of illness, environmental contacts, family history and a variety of other important clinical data. It should be appreciated that children with acute leukemia develop spontaneous remissions and remissions in response to chemotherapy much more easily than do adults. On the other hand, elderly persons with acute leukemia not infrequently are unchanged or worsen in response to therapy with conventional chemotherapeutic agents. Thus, the ratio of children to adults in any group of acute leukemia patients under study may profoundly influence the outcome of an evaluation study. The importance of the leukemia type is emphasized by the fact that acute lymphocytic leukemia at any age usually responds

better to therapy than any other type of acute leukemia. Patients with acute monocytic leukemia, in contrast, almost invariably respond poorly to all types of therapy.

Certain specific laboratory and cytologic characteristics of the leukemia may be of importance in consideration of therapeutic results. Some recent studies suggest that acute leukemia patients with leukopenia at the outset do better than those with an initial elevation of the white count.<sup>2</sup> Surprising also is the observation that acute granulocytic leukemia patients with blast cells containing Auer rods respond better to therapy than do those patients with blast cells devoid of Auer rods.<sup>4</sup> Therapeutic response in relationship to either the chromosomal or enzymatic characteristics of leukemia cells also may be important. For example, bulsulfan (Myleran) therapy probably is more effective in patients with chronic granulocytic leukemia whose leukemic cells contain the Philadelphia chromosome than in those who do not have this abnormality<sup>5</sup>.

## Chemotherapy

Recommended forms of chemotherapy are constantly under revision but recently promising results have added considerable substance to some of the newer concepts. In childhood acute leukemia high initial remission rates (80-90 per cent) are achieved with drugs that otherwise might be too toxic for prolonged periods of therapy. Once a child has experienced a remission, some less toxic chemotherapeutic drugs are used for maintenance therapy. There now is little doubt but that survival of patients on maintenance drug therapy is better than the survival of patients who are not maintained on chemotherapy during remission. It also now is quite clear that if relapse develops while on a particular drug it is most unlikely that that drug will ever be useful again. Although a variety of new drugs, new combinations of drugs, and new drug schedules have been tried in adult leukemia, little improvement over the old schedules has been attained.

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*Supported in part by Public Health Services Grants (HE-08493-02 and CA 08287-01) and in part by Public Health Service Training Grant (HE-5613-05) National Heart Institute, Public Health Service.*

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The five most commonly used drugs in the specific treatment of acute leukemia are prednisone, methotrexate (Amethopterin), 6-mercaptopurine (Purine-thol), vincristine (Oncovin) and cyclophosphamide (Cytoxan). The first three compounds mentioned have been used for the past 10 years or more and their use alone will not be discussed. Experience with the other two agents, however, has been only during the past several years.

Vincristine is a vinca-rosa alkaloid with properties which suggested initially that it would be of particular value in the treatment of the lymphomas. One of the most advantageous features of vincristine is its megakaryocyte sparing effect making it particularly useful when thrombocytopenia is a problem. Neurotoxicity associated with prolonged administration, however, limits its usefulness in lymphoma therapy but it has become important in the induction of remissions in children with acute lymphocytic leukemia.<sup>6</sup> Used in combination with prednisone, remission rates of 80 per cent or more are achieved in previously untreated patients.<sup>7</sup> Vincristine occasionally may induce remission in patients resistant to other forms of chemotherapy. Maintenance vincristine therapy during remission, however, is inadvisable because of the neurotoxicity problem.

Cyclophosphamide (Cytoxan) also is used principally in the treatment of the lymphomas, but it has limited value in the therapy of acute leukemia.<sup>8</sup> It is not particularly useful in the acute leukemias of adulthood but occasionally it will induce a remission of short duration. Cyclophosphamide has few properties that recommend it to the therapy of the acute leukemias of childhood. Bone marrow toxicity is somewhat erratic and alopecia is not an uncommon sequelae.

### **New Chemotherapeutic Regimens**

The simultaneous administration of several anti-leukemic agents has been under recent intensive investigation. The rationale behind combination chemotherapy is based on several concepts. There is evidence that the five commonly used anti-leukemic agents do not interfere with the action of one another.<sup>9</sup> In experimental leukemia it has been suggested that all leukemic cells within a specific animal may not respond to the same agent. The lack of indications for the selection of the appropriate chemotherapeutic agent when time is of the essence has made it clinically impractical to sequentially administer the available antileukemia drugs in most patients. Finally, there is the possibility that synergism or potentiation will enhance the beneficial pharmacological activities of drugs without proportionately increasing their toxicity.

Clinical trials with many combined treatment schedules now are in progress and new ones are being devised faster than the old ones are evaluated. One of the first major forms of combined therapy was developed at the National Cancer Institute and has become known as VAMP. The name is derived from simultaneous use of vincristine (V), amethopterin (A), 6-mercaptopurine (M) and prednisone (P). It is reported that VAMP is capable of inducing remissions in the majority of adult and childhood acute leukemia patients treated to date.<sup>10,11</sup> Although the initial remission rate is high it is discouraging that the duration of remission probably does not exceed that of other conventional forms of therapy. Others have not found this regimen particularly effective in adult leukemia.<sup>12</sup> As would be expected, the toxicity of this combined form of therapy is quite high. Recently, Thompson, Hall and Moloney have reported extremely high adult acute leukemia remission rates on a slightly modified VAMP schedule.<sup>13</sup> It was felt that the lowered dosages employed reduced drug toxicity.

Another form of combined therapy consists of the initial simultaneous use of vincristine and prednisone. Patients experiencing remission from these agents then are treated sequentially with methotrexate, 6-mercaptopurine and cyclophosphamide for two courses or cycles of therapy. This method of bi-cyclic therapy has been designated as the BIKE regimen.<sup>14</sup>

Other forms of combination therapy under investigation at present are POMP (similar to VAMP except that massive parenteral doses of all agents are used) and PAP (POMP without vincristine).<sup>12</sup>

Another approach to improving the therapeutic results in acute leukemia has been to vary rather drastically the duration and intensity of treatment with some of the standard chemotherapeutic agents. It now is thought that leukemic cells are most susceptible to destruction if they are exposed to adequate concentrations of toxic drugs just prior to mitotic division. On conventional schedules there may be long periods of active cellular division when drug levels are too low to be effective. Consequently, the new dosage schedules are designed to provide either intermittently higher or more sustained drug levels than are achieved by conventional schedules. Extremely promising results have been obtained with variations in the use of methotrexate. This agent acts by binding the intracellular enzyme, dihydrofolic reductase. This results in irreversible damage to the rapidly proliferating cells by blocking their ability to synthesize nucleoprotein. Early experiences with methotrexate indicated that leukemic cells although initially sensitive to its action, soon become resistant. Later it was suggested that either higher or more sustained initial blood levels

of methotrexate might more effectively destroy the leukemic cells. Thus, regimens have been devised which prescribe either periodic short intensive oral courses or intermittent parenteral injections of large doses.

Hugley has reported relatively high remission rates in a small series of adult patients with acute leukemia with short intensive oral courses of methotrexate.<sup>15</sup> He has employed repetitive 5 day courses or oral therapy every 6-8 hours alternating with 10 day periods of no therapy. Toxicity associated with this regimen has been high and quite unpredictable. This program deserves further evaluation.

Excellent results with a cyclic form of combined long term therapy have been reported by Zeluzer.<sup>16</sup> Following induction of remission with prednisone and 6-mercaptopurine, remissions are maintained in children with alternating 3 month courses of methotrexate and 6-mercaptopurine.

Considerable success has been achieved both in children and adults with bi-weekly intravenous injections of methotrexate.<sup>17</sup> Toxicity is low and the remission rate is quite high. The recently reported results of acute leukemia therapy in children consisting of an initial course of prednisone and vincristine followed by biweekly parenteral methotrexate are most remarkable.<sup>7</sup> Of the 80 per cent who initially enjoyed completed remission about 80 per cent are alive and well 24 months later.

### **New Chemotherapeutic Agents**

Two agents under clinical evaluation during the past few years are methylglyoxal-bis-guanylhydrazone (methyl-GAG) and hydroxyurea.<sup>18-19</sup> Although both agents have shown some activity in several forms of acute leukemia, especially in the blastic phase of chronic granulocytic leukemia, it appears that their extreme toxicity will limit their usefulness.

Cytosine arabinoside is a potent inhibitor of nucleic acid synthesis which shows some promise in the treatment of acute leukemia.<sup>20</sup> This compound almost invariably produces a megaloblastic anemia and varying degrees of thrombocytopenia. Ulceration of the gastrointestinal tract also may occur. Another agent of potential value is BCNU (bis chloroethyl nitroso urea). It is extremely active in rodent leukemia.<sup>21</sup> Although the hematologic response in some adult patients with acute leukemia has been favorable the delayed systemic toxicity of BCNU has been a serious problem.

### **Irradiation**

External irradiation has proven of limited value in the treatment of acute leukemia. Generalized irradiation may depress the bone marrow with resultant thrombocytopenia and bleeding, but selected local therapy may be of value. Local ir-

radiation often will resolve leukemic infiltrates in restricted areas, such as the skin, CNS, salivary glands, middle ear or tonsils. Recently, attempts to treat leukemia with extracorporeal irradiation have been reported.<sup>22</sup> The technique involved allowing the patient's blood to pass through a coil of tubing while exposed to ionizing radiation before it re-enters the body. To date, although the results of this form of treatment of patients with chronic lymphocytic leukemia have been encouraging, little success has been obtained in the treatment of acute leukemia.<sup>22</sup>

Enthusiasm has waned for the treatment of acute leukemia with total body irradiation followed by homologous bone marrow transplantation. In virtually all instances the transplanted bone marrow has been rejected and the leukemia has recurred. Recently, however, Mathe has reported some probable success with total body irradiation followed by an infusion of marrow obtained from several near relatives.<sup>23</sup> It is now apparent that a better understanding of basic immune mechanisms is a prerequisite to the further use of this form of treatment.

### **Supportive Therapy**

Patients with acute leukemia die almost invariably from either infection or hemorrhage.<sup>1,24</sup> The complications may be the consequence of either the leukemic process or vigorous chemotherapy. If supportive therapy will sustain these patients until either therapy is effective or there is marrow recovery, then life expectancy may be appreciably increased.

Infection is the primary cause of fatality amongst our acute leukemia patients.<sup>25</sup> Many succumb rapidly to organisms of low pathogenicity which flourish in the presence of an incompetent cellular defense mechanism.<sup>26,27</sup> Infection may develop abruptly or insidiously and differentiation between infection and the leukemic process often is most difficult. Many of the febrile events require the prompt institution of antimicrobial therapy after the appropriate cultures are obtained. Continuance or alteration of antimicrobial therapy is contingent on the results of the bacteriologic cultures.

The most common forms of bacterial infection in patients with acute leukemia at present are gram negative in type (proteus, coliform and pseudomonas).<sup>1,24</sup> In the past decade gram positive infections have become less prevalent due in a large part to the development of penicillins active against penicillinase producing staphylococci.<sup>28</sup> Local or disseminated fungal infections, especially those due to the candida group, have become a major problem.<sup>24</sup> The probability of gram negative sepsis always should influence the initial selection of anti-



biotics. The recent availability of cephalosporines along with such agents as kanamycin and colistin have helped to improve the outlook of leukemia patients with bacterial infections.<sup>29</sup>

Dramatic temporary control of infections in children with acute leukemia has been achieved through the transfusion of granulocytes obtained by means of plasmapheresis from patients with chronic granulocytic leukemia.<sup>30</sup> The transfer of greater than  $10^{10}$  granulocytes per square meter of body surface is necessary for therapeutic effectiveness. An adult male would require the white cells from 2-3 units of blood containing 200,000 leukocytes per cu. mm. in order to increase his peripheral white count by 1,000 per cu. mm. Only about 5 per cent of the transfused cells are accounted for in the circulation of the recipient. About 50 per cent of the transfused granulocytes are lost per day. The unavailability of adequate numbers of leukocyte donors makes these transfusions of little general practical value.

Isolation of acute leukemia patients from any bacterial organisms also is being explored as a means of prolonging life by preventing infections. Patients are rendered "germ free" with antimicrobial and antiseptic agents and are maintained in "life islands" (man sized versions of the plastic isolators used for germ free animal studies).<sup>31</sup> Some bacteria free patients with severely aplastic bone marrows have been maintained for several weeks under these circumstances. Plans for constructing large germ free rooms for several patients now are in progress. Although early results are encouraging the ultimate value of this technique is uncertain.

Protracted and severe bleeding in patients with acute leukemia almost invariably is the result of thrombocytopenia, usually with platelet counts below 30,000 per cu. mm.<sup>32,33</sup> The transfusion of adequate numbers of viable exogenous platelets will temporarily correct the thrombocytopenia and stop the bleeding. About 80 per cent of the platelets in carefully collected ACD blood not more than 6 hours old will be recovered in the blood of the transfused recipient. Platelet rich plasma (PRP) behaves in a similar fashion but the recovery of concentrated platelets is only about 50 per cent that of fresh whole blood or PRP. Similarly, the platelets in blood stored at 4° C for 24 hours is about 50 per cent as effective as fresh whole blood or PRP. The platelets in older bank blood are worthless. Some very recent studies indicate that further acidification of conventional ACD blood will decrease platelet stickiness so that the recovery and survival of platelets in platelet concentrates compares favorably with that of fresh whole blood or PRP.<sup>34</sup> The loss of transfused fresh platelets in the recipient is 30-50 per cent per day. Transfused older platelets will disappear much more rapidly.

The platelet count in a 70 kg. man will be increased about 12,000 per cu. mm. immediately following transfusion with 500 cubic centimeters of platelet rich plasma less than 6 hours old. The use of older blood or plasma or platelet concentrates requires the transfusion of more platelets to achieve the same initial result. When either anemia or hypovolemia as associated problems, fresh whole blood usually is administered initially. In most other settings platelet rich plasma or platelet concentrates are preferred. Except in extreme emergencies ABO and Rh compatible blood should be used.

A frequent finding in some forms of leukemia is the overproduction of uric acid either as a part of the primary disease or in relation to therapy. The major complications of hyperuricemia are secondary gout, renal calculi and even renal tubular obstruction. Previous prophylactic therapy employed to prevent the precipitation or urate stones consisted of the forcing of fluids and alkalization of the urine. A new and useful method of preventing such a complication is the use of allopurinol (Zyloprim). This agent decreases serum and urine uric acid levels by blocking the enzyme<sup>35,36</sup> xanthine oxidase which is responsible for the oxidation of hypoxanthine to uric acid.

As one reviews the recent advances in the treatment of leukemia it is apparent that some progress has been made in improving the prognosis of the leukemia victim. Perhaps the major contributions are the improvements in supportive measures. The newer methods of specific treatment may be of principle value in providing greater numbers of therapeutic options than ever have been available previously.

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# Negative Results: Gold Leaf In Cataract Surgery

Harry H. Mark, M.D.

■ The successful use of charged gold leaf in surgery was recently reported.<sup>1</sup> This report was received with enthusiasm as opening new vistas toward the elimination of sutures in general surgery.<sup>2,3</sup> The eye is an excellent organ on which to observe directly the fate of the new material. It therefore seemed desirable to test the charged gold foil in cataract surgery, in the hope that here too it would replace sutures. The results were thought to be of interest to the general surgeon as well as to the ophthalmologist.

## Material And Method

Following the procedure of Gallagher and Geschickter, commercial pure gold foil (No. 4, soft) \* was obtained. A rubber comb was sterilized by soaking it in Zephiran for 24 hours, and a camel hair brush was autoclaved with the surgical instruments.

Two female patients, age 62 and 65 years, were operated upon February 1965 for uncomplicated senile cataracts. A limbus based conjunctival flap 5 mm. in width was prepared. The anterior chamber was entered ab externo by a shelving incision with a knife, 2 mm. beyond the insertion of the conjunctiva to the cornea. A peripheral iridectomy was done, and the cataract delivered by tumbling with an erisophake. Three sutures of 6-0 chromic catgut were placed at 9:30, 12, and 2:30 o'clock. Two gold leaves, 5 x 5 mm. in size, were electrostatically charged by stroking the camel hair brush against the rubber comb. The charged gold was placed on either side of the 12 o'clock suture, so that 2 mm. of it rested on cornea and 3 mm. on sclera, bridging the incision. Once the leaf was adherent to the globe further charges were conferred on it with the brush to enhance this adhesion. The conjunctival flap was then pulled over the gold leaves and over the corneoscleral sutures, and sutured in place.

## Results

As soon as the gold was covered with conjunctiva its firm clutch to the globe seemed to loosen. In both cases the immediate postoperative course was mild. Neomycin with Dexamethasone ointment was

instilled once daily for three weeks. Two weeks postoperative the anterior chamber in both cases still had +2 cells. Atropine ointment was therefore added once daily. The anterior uveitis subsided in the first case after 5 weeks; and in the second after six. The usual conjunctival injection subsided, too, except around the buried gold. In one patient the gold then pierced the conjunctiva and finally fell out spontaneously at the end of the sixth week. In the second patient the gold extruded only partially, and was removed with forceps 9 weeks postoperatively. Visual recovery was not impaired.

The second patient received her permanent glasses one week before the remains of the extruding gold were removed.

## Comment

When a camel hair brush is stroked against a rubber comb it obtains a positive (+) charge. The living tissue is assumed to be negatively (-) charged. It was therefore said that the positively charged gold adhered to the tissue through electrostatic forces. This is true as long as the other surface of the charged leaf is exposed, hence its usefulness in covering skin defects.<sup>4</sup> If, on the other hand, the gold is covered by tissue, an electric circle is formed, and all charges cancel each other. This seemed to have been the case when the conjunctiva was pulled over the gold leaf adherent to the globe.

Gallagher and Geschickter used gold foil mainly to cover bleeding areas, and it is thus likely that the adhesion of the gold to the tissue was affected by other than electrostatic forces.

The eyes have tolerated the buried gold very well, although the postoperative anterior uveitis lasted longer than usual. No adhesions between the gold and surrounding tissue were observed. The foils finally extruded completely, leaving no permanent sequelae.

## Summary

Following a report on the utility of charged gold foil in general surgery, its fate in the eye was in-

\* Manufactured by The J. M. Ney Company, Hartford, Connecticut.

DR. HARRY H. MARK, assistant junior attending, St. Raphael Hospital, New Haven; associate, Charlotte Hungerford Hospital, Torrington; consultant, Litchfield County Hospital, Winsted, Connecticut.

vestigated. Electrostatically charged gold leaves were placed over the corneoscleral incision in two cases operated for cataract. Once covered with conjunctiva the gold seemed to lose its hold on the underlying tissue. It extruded spontaneously through the conjunctiva within nine weeks, leaving no sequelae.

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# Breast Problems And Oral Contraceptives:

## A Clinical Note

Jean E. Morin, M.D. and Ira S. Goldenberg, M.D.

■ The concern of modern man with overpopulation has led to the development of varied contraceptive methods. Mechanical devices to prevent conception have been used for many decades but in recent years numerous exogenous endocrine preparations have been developed to suppress ovulation "physiologically," and these have been widely accepted on grounds of convenience, esthetics and proven effectiveness. Physicians who prescribe these preparations, however, must weigh these three factors against the possibility of side effects as well as certain adverse physiological responses in individual patients.

Previous reports have suggested the development of problems such as thrombophlebitis resulting from use of these drugs but most have later been demonstrated to be fortuitous association. Nevertheless, during the past year the authors have encountered a considerable number of women receiving contraceptive drugs who presented themselves with abnormalities in breast tissue. Most women are aware of the high incidence of breast cancer and any breast tissue alteration creates immediate anxiety about cancer. This report is to call attention to the pathophysiological effects of the usual estrogen-progesterone contraceptive preparations on breast tissue and to emphasize that the physician must be prepared to deal with these alterations for as long as the medication is administered.

The following are synopses on three patients we encountered and have selected as typical of problems involved:

1. A 32-year-old mother of two children who had a long history of psychiatric disturbance. Eight months prior to our evaluation, a therapeutic abortion was performed on the basis of mental disturbance. An oral contraceptive had been prescribed after the abortion and it was continued for the eight-month period to the time of her initial visit to our clinic. During the early months of the drug administration, a pruritic dermatitis was noted over the left breast, abdomen, axilla and back, and for two weeks prior to evaluation, a small amount of yellowish discharge had been noted

emanating from the left nipple. There was no associated breast pain.

Physical examination revealed both breasts to be soft and non-tender but there was a diffuse nodularity present. A small amount of yellowish material could be expressed from the left nipple. There was no axillary adenopathy and mammography revealed no abnormality.

The contraceptive drug was discontinued following which the breast discharge ceased and the nodularity of the breasts cleared.

2. A 22-year-old woman who delivered a normal child seven months prior to our evaluation. The contraceptive was prescribed after delivery. After two months of therapy, the patient noticed left breast discomfort which she at first ignored but thereafter the breast became progressively more uncomfortable until she sought medical advice.

Physical examination revealed normal breasts save for fine nodularity bilaterally, more marked on the left side, and a small tender mass was palpable in the left breast. There was no lymphadenopathy. Mammography demonstrated no gross pathology.

The contraceptive was discontinued and the symptomatology promptly resolved.

3. A 22-year-old unmarried woman who had a history of premenstrual tension from menarche, manifested mainly by engorgement of her breasts which became tense and tender one week prior to each menstrual period. Dysmenorrhea was also present with local and systemic symptoms. To reduce these problems, an oral contraceptive preparation was prescribed by her physician several months before our evaluation. Two months prior to evaluation, breast tenderness became a constant symptom and a small mass was noted in the right breast. The mass was most marked in both size and tenderness immediately prior to menstruation. No nipple discharge had been noted.

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Physical examination revealed bilateral nodularity of the breasts and marked tenderness of one nodule in the right breast. There was no lymphadenopathy. Mammography demonstrated no abnormal masses.

The hormonal preparation was discontinued with rapid clearing of the breast nodularity.

### Discussion

In 1889, Schinzinger first called attention to the relationship between the ovaries and the breasts, particularly as related to breast cancer. He could not define precise mechanisms of association and it was not until 1900 that Knauer first demonstrated the endocrine activity of the ovary by use of autotransplantation techniques. In 1923, Allen and Doisey laid the foundations for modern gynecological endocrinology by inducing estrus in immature animals using a potent ether extract of liquor folliculi aspirated from hog ovaries. The associated effects on breast tissue were clarified in succeeding years and it is now recognized that ovarian estrogen and progesterone each induce specific changes in mammary tissue. These changes include growth and development of the alveolo-lobular and ductal systems. Postpartum lactation, however, is induced solely by pituitary activity. The cyclic interplay between the hypophysis and the ovary is responsible for ovulation and menstruation, cycles in which mammary gland alterations participate preparatory to further development of the breasts during pregnancy and subsequent lactation. It must be accepted that administration of estrogen-progesterone combinations, which have the physiological effect of suppressing pituitary induction of ovulation while at the same time maintaining regular men-

struation, will also involve intermittent mammary tissue changes. This is not a side effect of the contraceptive drug but rather a physiologic effect which must be anticipated.

Tender breasts which become nodular due to proliferation of alveoli and ducts and do not regress with induction of "artificial" menses alert the patient that something is amiss. Fear of cancer, enhanced by educational programs for detection, becomes overtly manifest and anxiety increases. Examination by a physician confirms the presence of diffuse breast nodularity and a decision must be made as to the need for surgical biopsy. It is difficult for a surgeon to decide what, if anything, should be biopsied.

As the use of contraceptive drugs intensifies, increasing numbers of patients are presenting with these problems and the physicians' dilemma with respect to management of such women is increasing proportionally. At present, however, when a patient presents with breast masses, it seems imperative to ascertain whether contraceptive medication is currently being taken or has recently been discontinued. Cessation of the drug will usually bring about regression of drug-induced changes within a few weeks so that pathological entities can be better delineated. Occasionally, biopsy of a particularly suspicious lesion may be necessary before drug cessation, but in most instances it can safely be delayed until medication effects have regressed and more normal breast tissue status restored. Breast cancer can coexist with benign breast disease, irrespective of the etiology of the latter, and it is of the utmost importance that all breast tumors be completely evaluated lest cancer be overlooked.

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Never mistake common sense and tact for dishonesty and deceit but always remember the possible dire consequences of showing the pity you may feel for an incurably ill patient and the tragedy that must result if he rather than a responsible member of his immediate family is frankly told the truth when hope alone may be the feeble flicker that sustains Life.—Henry V. Hopkins, *Principles and Methods of Physical Diagnosis*, p. 2, W. B. Saunders Company, Philadelphia and London, 1965.



# THE PRESIDENT'S PAGE

## A Pause To Honor, To Reflect And To Wonder

ON June 20th the physicians of Litchfield County and elsewhere in Connecticut, with their wives and guests, took time from their practices to attend the Bicentennial Celebration at Hotchkiss School, Lakeville, Connecticut. This gathering convened to commemorate the founding in 1767 of the Litchfield County Medical Association as a pioneer organization conceived prior to the Revolutionary War and persisting through the present period of implementation of national legislative measures which many consider a revolution in medical care. In addition to the observance of this milestone by appropriate ceremonies, it was an expressed purpose of the meeting to provide an opportunity to survey the vast progress made by the medical profession during this span of 200 years and for rededication of the members to the continuation of the highest quality of medical care under the free enterprise system.

Those who drove on that morning along the winding roads through the hills glimpsing the panorama of the verdant countryside unfolding its everchanging pastoral scenes began the day with a refreshing treat. One passed houses more than a century old which had been the residences of illustrious doctors in these rural communities and of their patients who had contributed much to our nation. Stopping at a famed inn which had served many of them in the past, it was inevitable that one would recall tales of the drama of their lives and times. It provoked a degree of sadness to be shaken from this contemplative mood by the tolling of the village church bell to announce that suddenly it was 9:00 a.m. in 1966 and to remind us that, as much as we might enjoy nostalgic reveries of life of the past, realities of the present were upon us to be faced.

It was fitting that the convocation was held at an institution which stands as an edifice of progress in education at a level whose significance is often lost sight of in the long trail of learning the potential doctor must follow and especially in a building dedicated to "Whit" Griswold who, as President of Yale, gave new life to the so-called "secondary schools." What we were to experience on this day was an extension of the continuing process of education essential to all physicians. The symposium included documentary historical resumes and references to legacies of past contributions to clinical medicine. It is anticipated that these will be recorded in detail in a later issue of CONNECTICUT MEDICINE

In forecasting the future, a well-qualified participant brought into sharp contrast the nature of the practice of medicine during the past centuries with those changes in medical care which may occur as a result of burgeoning scientific knowledge and rapid developments in technology. While calling attention to the impending age of the computer, the availability of batteries of diagnostic tests, and the application of the team-approach in an era of increasing specialization, he noted the continued value of the experienced judgment of the individual doctor and need for preservation of the personalized patient-physician relationship.

Sprinkled with pleasant social activities, and climaxed by an evening reception highlighted by the conferring by the Connecticut State Medical Society of three Honorary Memberships and two Honorary Degrees in Medicine upon citizens who have made notable contributions to medicine, the historic celebration was indeed a memorable occasion.

It is hoped that doctors, in cooperative efforts exemplified in the past by the Litchfield County Medical Association, will exercise similar zeal in the next century to meet the medical needs of the public.

ORVAN W. HESS, M.D.



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**Dextro-amphetamine sulfate:** Insomnia, excitability, and increased motor activity are common and ordinarily mild side effects. Confusion, anxiety, aggressiveness, increased libido, and hallucinations have also been observed, especially in mentally ill patients. Rebound fatigue and depression may follow central stimulation. Other effects may include dry mouth, anorexia, nausea, vomiting, diarrhea, and increased cardiovascular reactivity.

**Meprobamate:** Drowsiness may occur and can be associated with ataxia, the symptom can usually be controlled by decreasing the dose, or by concomitant administration of central stimulants. Allergic or idiosyncratic reactions: maculopapular rash, acute nonthrombocytopenic purpura with petechiae, ecchymoses, peripheral edema and fever, transient leukopenia. A case of fatal bullous dermatitis, following administration of meprobamate and prednisolone, has been reported. Hypersensitivity has produced fever, fainting spells, angioneurotic edema, bronchial spasms, hypotensive crises (1 fatal case), anuria, stomatitis, proctitis (1 case), anaphylaxis, agranulocytosis and thrombocytopenic purpura, and a fatal instance of aplastic anemia, but only when other drugs known to elicit these conditions were given concomitantly. Fast EEG activity, usually after excessive dosage. Impairment of visual accommodation. Massive overdosage may produce drowsiness, lethargy, stupor, ataxia, coma, shock, vasomotor, and respiratory collapse.





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11:47 pm



11:53 pm



12:06 am

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| FORMULA— | Alcohol . . . . .                   | 70% |
|          | Benzocaine . . . . .                | 10% |
|          | Chloroform, 4 mins. per fluidounce. |     |

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By providing more comfort and extra sleep for the baby, DENTOCAIN LOTION MILD grants the mother greater peace of mind and several additional hours of necessary rest.

DENTOCAIN ADULT is also useful in providing temporary relief for pain of adult toothache.



**Dentocain Co., Bloomfield, Conn., U.S.A.**

Professional samples and descriptive literature sent on request.



# **FORTY-FIRST CONNECTICUT CLINICAL CONGRESS**

**of the  
CONNECTICUT STATE MEDICAL SOCIETY  
and the  
YALE UNIVERSITY SCHOOL OF MEDICINE**

**Yale-New Haven Medical Center — Mary S. Harkness Memorial Auditorium  
333 Cedar Street, New Haven**

**Wednesday, September 28, 1966**

9:00 Registration (Coffee will be served in the lobby until 9:30)

## **Morning Session**

9:45 WELCOME AND OPENING REMARKS—  
Orvan W. Hess, *President Connecticut State Medical Society*

## **RECENT ADVANCES IN DIAGNOSIS AND MANAGEMENT OF LIVER DISEASE**

Gerald Klatskin, *New Haven, Presiding*

10:00 DIAGNOSTIC PROCEDURES  
William A. Tisdale, *Burlington, Vermont*

10:30 SURGICAL MANAGEMENT  
Louis M. Rousselot, *New York City*

11:00 PANEL DISCUSSION AND QUESTIONS  
Moderator: Gerald Klatskin  
Panelists: William A. Tisdale and Louis M. Rousselot

11:45 INTERMISSION

12:00 CLINICAL PATHOLOGICAL CONFERENCE  
Philip K. Bondy, *New Haven, Presiding*  
Pathologist: Averill A. Liebow, *New Haven*  
Radiologist: Arthur R. Clemett, *New Haven*  
Discussant: Gerald Klatskin

1:00 LUNCHEON

## **Afternoon Session**

## **RECENT ADVANCES IN DIAGNOSIS AND MANAGEMENT OF THROMBOEMBOLISM**

Stephen B. Sulavik, *New Haven, Presiding*

2:30 PROBLEMS OF DIAGNOSIS  
Arthur A. Sasahara, *Roxbury, Massachusetts*

3:00 MEDICAL MANAGEMENT  
Myron Stein, *Providence, Rhode Island*

3:30 SURGICAL MANAGEMENT  
Ralph A. Deterling, Jr., *Boston, Massachusetts*

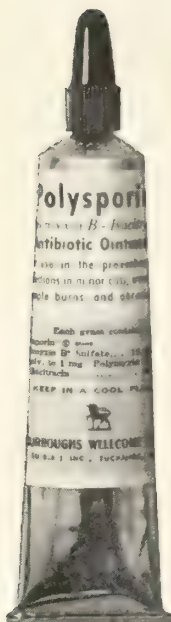
4:00 PANEL DISCUSSION AND QUESTIONS  
Moderator: Stephen B. Sulavik  
Panelists: Arthur A. Sasahara, Myron Stein, and Ralph A. Deterling, Jr.

Luncheon for visiting physicians will be served in the cafeteria of the Yale-New Haven Hospital, Memorial Unit.

The registration fee of \$5.00 provides for admission to all sessions of the Congress. Hospital residents and interns and medical students will be admitted without charge, if a statement of their position, signed by an official of the hospital or school, is presented at the registration desk.

## **PLAN NOW TO ATTEND**

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# FROM THE GENERAL MANAGER'S OFFICE

WILLIAM R. RICHARDS, M.D., *General Manager*

Peter F. Villano  
*Director of Public Relations*

160 St. Ronan Street, New Haven, Conn.  
Telephone 865 0587

Josephine P. Lindquist  
*Assistant to General Manager*

## SUMMARY OF COUNCIL ACTIONS

**Wednesday, July 14, 1966**

### I. Attendance

Present in addition to the Chairman, Dr. S. J. Martin, were: Drs. Hess, Bradley, W. Martin, Goldberg, Brandon, H. Caplan, M. Caplan, Polivy, Rogol, Grendon, Egan, Abbot, Spitz, Shepard, Ayres, Cramer, Fabro, Grant, and Pelz. Also present were: Mrs. Lindquist, Mr. Villano and Dr. Richards. Absent were: Drs. Gardner, Weise, Sr., Hastings, Nolan, Ciccarelli, Petrie, Wilson, Palomba and Roch.

### II. Routine Business

#### Approval Of Minutes

As printed and distributed, it was VOTED to approve the minutes of the meeting of May 25, 1966.

#### Life Memberships

It was VOTED to approve applications for Life Membership received from the following Active Members of the Society:

Frank Mongillo, 5 Elm Street, New Haven (NHCMA)

Edwin G. Reade, P. O. Box 226, Watertown (LCMA)

Charles T. Schechtman, 62 Dover Road, New Britain (HCMA)

Morris Slater, 1100 Dixwell Avenue, Hamden (NHCMA)

#### Student Membership

It was VOTED to elect to Student Membership the following Connecticut resident who is attending the school of medicine indicated:

Dominic Michael Erba, 137 North Street, Hamden

Pre-Med: St. Michael's College

University of Rochester—Class of 1969

Parent: Andrew F. Erba

#### Appointment Of Representative—AMA Conference On Rehabilitation

It was VOTED to request Kurt Pelz, Wallingford, to attend this Conference as a representative

of the Society. The Conference will be held at Chicago, September 8-9, 1966, and the AMA will assume the travel expenses of the representative.

#### Representative—Governor's Advisory Panel On Exceptional Children

In response to a request from Governor Dempsey that the Society appoint a qualified representative to serve with an Advisory Panel to Study Legislative Needs for the Education of Exceptional Children, it was VOTED to direct the Chairman, Dr. Martin, to discuss the request with the Governor and select a suitable CSMS member to serve on the Panel. Time being short (meetings of the Panel to begin on July 15), the selectee of the Chairman is to be appointed without further action by the Council.

#### Representative—R.I. Conference On Medical Aspects Of Sports

On recommendation of the Committee on Accident Prevention, it was VOTED to authorize Isao Hirata, Jr., New Haven, to attend the 5th Postgraduate Conference on the Medical Aspects of Sports, Kingston, Rhode Island, August 18-19, 1966, and to reimburse Dr. Hirata for usual expenses plus the tuition fee of \$35. The Committee, of which Dr. Hirata is a member, is planning a Connecticut conference of similar nature to be held later this year. A report to the Council on the proceedings of the Conference is expected.

#### Representative—AMA Regional Conference On Disaster Medical Care

It was VOTED to authorize John Shoukimas, Hartford, Chairman of the CSMS Committee on Disaster Medical Care, to attend this Regional Conference, Boston, July 23-24, 1966, as a representative of the Society, and to reimburse Dr. Shoukimas for usual expenses incurred by his attendance. A report to the Council on the proceedings of the Conference is expected.

#### Date Of Next Meeting

It was VOTED to authorize the Chairman, in consultation with the General Manager, to call the next meeting at such time as the amount of business to be considered is sufficient.

### **III. Old, New And Special Business**

#### **Report—AMA Conference Of State Society Mental Health Representatives**

James C. Johnson, Jr., Hartford, a member of the CSMS Committee on Mental Health, filed a report on the proceedings of the 12th Annual Conference of Mental Health Representatives of State Medical Societies, Chicago, March 18-19, 1966, which he attended at the request of the Council. It was VOTED to accept Dr. Johnson's report, with commendation, and to assure that all members of the CSMS Committee on Mental Health receive copies of same for their information.

#### **Report—CSMS Delegate To The New Hampshire Medical Society**

Charles C. Verstandig, New Haven, filed a report on the proceedings of the New Hampshire Medical Society meeting (held jointly with the Vermont Medical Society), Wentworth-by-the-Sea, New Hampshire, May 22-25, 1966, which he attended as CSMS Delegate. It was VOTED to accept Dr. Verstandig's report, with commendation, and (since his service as a Delegate is now concluded) to thank him for serving the Society well as an official representative.

It was further VOTED to inform the New Hampshire and Vermont Medical Societies of the Council's reaction to, and concern with, the VMS decision (noted in Dr. Verstandig's report) to make the results of the VMS membership "fee profile" survey available to Blue Cross-Blue Shield (serving both Vermont and New Hampshire) but *not* to "other non-profit organizations, private insurance carriers or to physicians as individuals or groups . . .". Commending the joint intent of the Societies that the profile "not be used to establish a so-called 'fee schedule'," the Council expressed doubt as to the wisdom of limiting availability of the profile to the Blues and excluding other recognized third party agencies.

#### **Report—CSMS Delegate To The Medical Society Of New Jersey**

E. Tremain Bradley, Norwalk, filed a report of the proceedings of the 200th annual meeting of the MSNJ, Atlantic City, May, 1966, which he attended as a CSMS Delegate. It was VOTED to accept Dr. Bradley's report, with commendation, and to call it to the attention of the members of the Ad Hoc Committee on Administrative Organization and Planning, who presently have under study ways and means of improving and making more effective meetings of the CSMS House of Delegates.

#### **Report—Committee On Cooperation With The Yale School Of Medicine**

Edward Nichols, Hartford, Chairman of the CCYSM, filed a report on a meeting (4/28/66) of the Committee with their counterparts from Yale, at which plans for implementing P.L. 89-239 (the DeBakey legislation on heart disease, cancer, stroke, and related diseases) were reviewed. It was VOTED to accept Dr. Nichol's report, with thanks, as information, and to request him and the members of the Committee to keep the Council informed of progress with P.L. 89-239 on a continuing basis, particularly with respect to plans for assuring a maximum amount of participation by physicians engaged in the private practice of medicine.

#### **Report—Council Representative To Meeting Of The American College Of Surgeons**

As requested by the Council (5/25/66), Charles Polivy, Hartford, filed a report on the proceedings of an organizational meeting (to form a Connecticut Chapter) of the American College of Surgeons, New Haven, June 2, 1966. It was VOTED to accept Dr. Polivy's report, with thanks, as information, noting that a Connecticut Chapter of ACS has now been formed as a "forum for consideration of matters of ethical, economic, social and political importance affecting the care of the surgical patient" and that the audience (of ACS members) "was pleased to know of the Council's interest . . . and invitation (to ACS) to work with the Advisory Committees of CSMS in the pursuit of (the Chapter's) purpose."

#### **Report—Delegate To The Maine Medical Association**

Sydney Luria, Bridgeport, filed a brief report on the annual meeting of the Maine Medical Association, June, 1966, which he attended as a Delegate from CSMS. It was VOTED to accept Dr. Luria's report, with thanks, as information.

#### **Selection Of Date And Place For 1967 Annual Meeting**

After considering all reasonable alternatives presently available, it was VOTED to hold the 1967 Annual Meeting at the Statler Hilton Hotel, Hartford, April 25-27, 1967.

#### **Report—Committee On Building Management**

The Committee, having reviewed the premises of the Society's headquarters building, recommended that the building be painted, inside and out, and that certain alterations and refurbishing be undertaken. Accepting the Committee's report, including a choice (among five bidders) of a painting contractor, the Council VOTED to authorize the expenditure of up to \$6,000 of funds set aside



for Building Depreciation for the redecorating, alterations, etc. recommended by the Committee.

#### **Request—Committee On Postgraduate Education**

It was VOTED to approve a request of the Committee that authorization be given to dedicate the 1966 Clinical Congress to the memory of John C. Leonard, M.D., Hartford, late Director of Medical Education at the Hartford Hospital and Clinical Professor of Medicine at the Yale School of Medicine, and longtime active member of the CSMS Committee on Postgraduate Education.

#### **Report—Committee On Aging**

The Committee on Aging filed a comprehensive report on its study of the problem of arranging utilization review committee coverage for extended care facilities in Connecticut. The report was drafted after lengthy discussions were held with representatives of the Connecticut Chronic and Convalescent Hospital Association, the State Health Department (which certifies nursing homes for participation in Medicare A), and others.

Acting on the three major sections of the report, the Council VOTED:

(a) To approve a series of six "principles" formulated by the Committee recommended, as guidelines for utilization review committees for extended care facilities, as follows:

1. The Committee on Aging hereby goes on records as underwriting the principle of the private practice of medicine and the total responsibility of the physician for the care of his patient without interference and modification by third parties.

2. The Committee on Aging goes on record as approving the principle of utilization committees for extended-care facilities.

3. The validation for the care of patients in extended-care facilities (ECF) shall be determined by the utilization committees composed of physicians only, in the best interest of all patients.

4. The Committee on Aging has been charged by the Council of the Connecticut State Medical Society with the responsibility for setting up guidelines under which utilization committees for extended-care facilities will function.

5. The Committee on Aging of the CSMS approves of the reimbursement of physicians serving on utilization committees in extended-care facilities, such reimbursement to be charged to the government or appropriate fiscal intermediary as a compensable cost of hospital care under parts 18A and 19, P.L. 89-97.

6. The Committee on Aging recognizes the need for communication between this committee and

the physicians of Connecticut to promote the recognition of their obligation to provide:

- 1) continued high quality medical care and,
- 2) compliance with the principle established above.

(b) To authorize the Committee on Aging, on request, to assist an extended care facility or a related group of extended care facilities to obtain a satisfactory utilization review committee, composed of physicians, and to contact, when necessary, county medical associations and/or local medical societies for the purpose of obtaining their cooperation in finding physicians willing and able to serve on such committees for extended care facilities in the county or local area concerned.

(c) To authorize the publication in the Journal of a suitably-worded notice (to be worked out jointly by Dr. Pelz and the General Manager) urging physicians to report to the Committee on Aging instances in which it is believed that old people are being taken advantage of or are not getting value received from the providers of goods and services.

#### **Formation—A Fiscal Advisory Committee To The Council**

Acting on a suggestion offered by Charles Polivy, Hartford, it was VOTED to authorize the formation of a "fiscal advisory committee," its functions to include furnishing continuing advice to the Council on all fiscal matters and to serve as the budget committee which advises the Council concerning the preparation of the annual budget and the fixing of membership dues for each ensuing fiscal year. It was further VOTED to direct the Chairman of the Council to appoint such a committee, and to name the Treasurer the chairman thereof. In brief, it is intended that the committee shall (in addition to its duties as the budget committee) give prior review to all proposed expenditures which are not specifically provided for in the budget, and to make recommendations to the Council concerning same.

#### **Review Of Malpractice Suits In Connecticut**

Introduced by J. Alfred Fabro, Torrington, it was VOTED to adopt a motion as follows:

IT IS MOVED: That the CSMS Conference Committee with the Connecticut Bar Association submit a report to the Council, in a reasonable time as determined by it, preferably within the year, on medical malpractice in Connecticut.

It would include, but not be restricted to the following:

- (1) The number of cases in Connecticut during the last several years.

(2) Whether the legal suits in malpractice are or are becoming a problem, or are increasing.

(3) Does the Committee believe we in Connecticut should adopt a plan for "impartial" testimony as has been adopted by the Medical Society and the Supreme Court of New Jersey? The principle of "nonpartisan" panels has been endorsed by the A.M.A. (1961).

(4) Any information or suggestions as to the relationships of insurance carriers to the profession, and as to the relationships between the legal and medical professions in this field.

(5) Any recommendations and information which the Committee feels should be of interest or help to the Council in fulfilling its responsibility to the legal and medical professions and to the public in this field.

#### **Resolution—Cancer Coordinating Committee**

As proposed by the CSMS Cancer Coordinating Committee, it was VOTED to adopt a resolution concerning the Connecticut Tumor Registry which "resolves" that all physicians be urged to continue to report cases of neoplastic disease to the Registry (diagnosis, therapy, follow-up, etc.), particularly with reference to the therapy and progress of patients treated on an outpatient basis (in the physician's office, etc.) with radiation and the newer chemical agents. As adopted, the resolution will be embodied in a letter to be sent to all practitioners by the State Health Department, and will also be featured in an early issue of the Journal.

Pursuant to the discussion prompted by the resolution, it was further VOTED to inquire of the Tumor Registry what provisions are made for following registered patients who leave Connecticut and, conversely, what provisions are made to pick up cases coming to Connecticut from other places.

#### **Proposal—Office Of Dependents Medical Care**

Having been informed that legislation is now under consideration by the Congress to expand the scope of the DMC Program (formerly Medicare) by adding outpatient services for the dependents of active military personnel, care for the mentally retarded and physically handicapped children of active personnel, and comprehensive medical care for retired personnel and *their* dependents, the Council was asked by ODMC officials if the Society would "desire to continue its contractual relationship (with ODMC) in the administration of the expanded program."

Noting that authorization to expand the Program had apparently not yet been granted by Congress, the Council VOTED to refer the proposal to the Advisory Committee on Dependents Medical Care Program for study and report, informing the Committee that the Council is disposed *not* to

favor such expansion or to consider such expansion unless and until ODMC has agreed to adopt reimbursement policies which are in keeping with the Society's principles of "usual and customary fees, as determined at local level."

#### **Request For Opinion—CSMS Section On Orthopaedics**

Notice was received from Charles T. Flynn, Jr., Meriden, Secretary, that the members of the Section on Orthopaedics feel that the Section might "achieve better identification and stature" if it were known as "The Connecticut Orthopaedic Society" and request the opinion of the Council as to whether such a change in name would be permissible under the CSMS bylaws. Assurance was given that the Section wished "to remain, as always, a sub-group of the parent organization (CSMS)."

Voicing no objection to the proposal, as such, the Council VOTED to convey to the Section the opinion that the present bylaws require that sections of the Society be called "Sections," and, therefore, that the proposed change in name to "The Connecticut Orthopaedic Society" would not be permissible.

#### **Resolution—CSMS Section On Orthopaedics**

Proposed by the Section, it was VOTED to adopt a resolution on automotive safety legislation as follows:

Whereas: The number of people killed in traffic accidents has increased 18 per cent in the past three years; and

Whereas: This unprecedented traffic toll has occurred in spite of the vigorous and faithful efforts of the National Safety Council, its local chapters, the multitude of state and local police authorities, and many other public and private agencies that have worked for improved traffic safety; and

Whereas: The development and use of automotive safety devices and design features has received little attention or use by the motoring public; and

Whereas: Legislation has been the only successful means of introducing safety devices and design features as evidenced by safety belts which are installed in all new cars and are legally required in 24 states; and

Whereas: The Federal government has established safety standards for government-purchased cars beginning with the 1967 models; and

Whereas: The Federal government is diligently developing and revising these standards as new knowledge is made available through research and experience; and

Whereas: These standards will reduce the incidence of accidents and severity of injuries caused by accident; therefore be it



Resolved: That the Connecticut State Medical Society vigorously support the legislation which will apply safety standards to all new cars and which will design and test a prototype safety car and thus develop new safety standards; and be it further

Resolved: That the Connecticut State Medical Society through our elected delegates submit a similar resolution to the American Medical Association House of Delegates at its next regularly scheduled meeting and that copies of this resolution be sent to President Johnson and Governor Dempsey.

#### **CSMS Policy On Direct Billing Under Medicare B**

Having heard the reports on pertinent actions of the AMA House of Delegates (June 26-30), and having reviewed present policies of the Society with respect to acceptable and preferred methods of reimbursing physicians for their services under all government-operated medical care programs, the Council VOTED to adopt a motion on "direct billing" as follows:

It Is Moved: That the Council of the Connecticut State Medical Society find that direct billing of the patient by the physician for services rendered under Part B of the Medicare Law, being both legal and ethical, is the preferred method of obtaining reimbursement for such services; and it is further

Moved: That the Council strongly commend such direct billing to the members of the Society as the preferred method for their use, and through CONNECTICUT M.D. and CONNECTICUT MEDICINE, fully inform the members of the advantages to the physician and the patient of direct billing vs. the acceptance of assignment of benefits.

N.B.: *The foregoing is a summary of the proceedings and actions of the Council on July 14, 1966. Detailed minutes of the meeting are on file at 160 St. Ronan Street, New Haven, for perusal by any interested member of the Society.*

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#### **PLACEMENT WANTED**

G.P.—with 2 years training in Internal Medicine, 8 years practice in medicine, wishes opportunity as associate in Southern Conn. Will consider salaried position leading to partnership or position in Industrial Medicine or a hospital appointment.

OBS.-GYN.—35 years of age, Board eligible, military obligations completed. University trained, would like to form either an association or join a group practice.

ANESTHESIOLOGIST—40 years of age, Board eligible, Connecticut license. Military obligations completed, would like to associate with another physician or in an institution.

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#### **PLACEMENT OPPORTUNITIES**

PEDIATRICIAN—Another Pediatrician to join a multi-specialty group in New Britain. Board certification or eligibility and Connecticut license or eligibility for licensure required.

G.P. OR INTERNIST wanted for full-time or part-time practice with another physician in the Stratford, Connecticut area. No investment needed. Net income \$25,000 to \$35,000.

MEDICAL EDUCATION DIRECTOR — Full-time Director wanted for 190-bed expanding hospital that will include 400 beds. Salary open. Report to Chairman, Medical Education Committee, Mt. Sinai Hospital, Hartford, Connecticut 06112.

WANTED—General Practitioner or Internist for General Medical and Surgical Accredited State Veterans' Hospital. Duties are those of ward officer on a general medical ward. Older physicians are acceptable, many fringe benefits such as housing and maintenance are at minimal cost. Salary range \$13,040 to \$17,040. Apply: Personnel Officer, State Veterans Home & Hospital, Rocky Hill, Connecticut.

PSYCHIATRIC RESIDENCIES available in a state hospital, comprehensive treatment facility for Central Conn. area, associated with Yale University Department of Psychiatry & Neurology, which provides supervision in hospital and opportunities for training in areas of special interest. Psychoanalytic training available at Western New England Psychoanalytic Institute. Personal analysis encouraged and can be arranged. Salary scale: 1st Year, \$8160 to \$8800; 2nd Year, \$8400 to \$9440; 3rd Year, \$9180 to \$11,100. Many fringe benefits, openings available at 1st, 2nd and 3rd Year levels. Please send full resume with first letter to John F. Lowney, Jr., M.D., Superintendent, Connecticut Valley Hospital, Box 351, Middletown, Conn.

PSYCHIATRIST — Needed for a community oriented mental hospital, to direct service within a 300-bed comprehensive mental health unit, which is one of several in a 2,000 bed State mental hospital. Opportunity for teaching, clinical work and research. Has to develop and direct team of social workers, psychiatric residents, psychologists and more than 80 nursing staff personnel. O.P.D., day care, in-patient consultation and emergency care available. Opportunity for association with Wes-

Ievan, Yale and University of Conn. Salary: \$14,240-\$20,000, depending on qualifications and experience. Excellent fringe benefits and annual leave to attend medical conventions. All particulars should be in first letter, including references. Apply—John F. Lowney, Jr., M.D., Supt., Connecticut Valley Hospital, Middletown, Conn. 06458.

**PATHOLOGIST**—Full or half-time to direct clinical laboratory in a 2300-bed mental hospital. Ample opportunity for research and teaching available. Well equipped and staffed laboratory, emphasis on neuropathology. Board certified or eligible pathologist preferred. Salary: \$14,740-\$19,000. Excellent fringe benefits. All particulars and references should be sent in first letter. Contact John F. Lowney, Jr., M.D., Supt., Conn. Valley Hospital, Box 351, Middletown, Conn. 06458.

**CLINICAL DIRECTOR**—To develop medical program in psychiatric hospital with emphasis on psychosomatic medicine. Opportunity for experience in employees' health clinic, workmen's compensation, clinic and psychophar, acologic drug research. Will direct department staffed by seven physicians. EEG, EKG, Radiology. Ophthalmology Depts. already fully equipped and staffed. Consultants available in all medical and psychiatric specialties. Salary: \$15,460-\$20,000, excellent fringe benefits, annual leave to attend medical conventions. All particulars and references should be included in first letter. Apply—John F. Lowney, Jr., M.D., Supt., Conn. Valley Hospital, Box 351, Middletown, Conn. 06458.

ANYONE INTERESTED IN THE ABOVE IS ASKED TO CONTACT THE GENERAL MANAGER'S OFFICE, 160 ST. RONAN STREET, NEW HAVEN, CONNECTICUT 06511.

### The Paper Jungle Of Drug Research

To a member of the clinical research staff of a pharmaceutical manufacturer the impact of the new drug law and F.D.A. regulations has been overwhelming. The immediate and unprinted reaction reflects the enormous increase in paper work and the infinite detail that are now demanded of the individual responsible for the clinical development of a drug for a pharmaceutical manufacturer . . . You have all been regaled by accounts of the size of the current new drug applications. Our latest weighed 550 pounds, and is by no means a record. Sending in supplementary case data on that particular application involved reproducing, collating and forwarding over 80,000 individual sheets of paper—Irwin C. Winter, Ph.D., M.D., in *Journal of New Drugs*, 4:6 (Nov.-Dec) 1964.

## Homosexuality Needs Understanding Treatment

Physicians should be prepared to give understanding treatment to homosexuals, and at the same time realize the discouragingly small chance for their rehabilitation, says an article in the current *Journal of the American Medical Association*.

Medical literature suggests that only about one in four homosexual patients are "cured" by psychiatric treatment—that is, returned to heterosexual interests, said Philip H. Heersema, M.D., of the Department of Psychiatry, Stanford University Medical School, Stanford, Calif.

Treatment is needed, however, because homosexuality is a vast and probably increasing problem, said a *Journal* editorial.

The treatment of a homosexual is almost entirely psychological, Dr. Heersema said. It "cannot be defined by what the physician does or says, but is defined by what he is to the patient."

Homosexuality should be designated an illness, not an elected "way of life," the doctor pointed out. The homosexual is one whose personality growth was arrested or has regressed to an adolescent level.

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HOSPITAL OF ST. RAPHAEL

REPORT OF PERINATAL MORTALITY AND MORBIDITY COMMITTEE

Calendar Year Of 1964

This is the 7th annual report of this committee. We have been meeting regularly every two months to discuss and review every perinatal death (from the 20th week of gestation through the 28th post partum day) and to attempt to evaluate in particular those deaths which are considered preventable or possibly preventable. Thus we might be able to offer recommendations to help reduce these preventable deaths.

The committee members have been consistently loyal in their attendance at these meetings. In addition there has been a lively interest on the part of the Obstetric and Pediatric house staffs, nurses and the sister supervisor of Obstetrics who are always invited and who contribute considerably to our discussions about perinatal deaths. At times other guests are invited, such as the chiefs of Obstetrics and Pediatrics and individual obstetricians who might have a special interest or be involved with a particular case.

The following statistics have been gathered for the year 1964.

|                             |                     |
|-----------------------------|---------------------|
| Total Livebirths            | = 2410              |
| Total Stillbirths           | = 42                |
| <hr/>                       |                     |
| Total Infants Delivered     | = 2452              |
| (Prematures ( 186           | = 7.7%              |
| <hr/>                       |                     |
| (1963                       | = 11.8%             |
| (1962                       | = 6%                |
| <hr/>                       |                     |
| Deaths (Neonatal (Newborns) | = 42                |
| (Fetal (Stillbirths)        | = 42                |
| <hr/>                       |                     |
| Total                       | 84 (corrected = 75) |

NOTE: The corrected figure is the result of questionable cases where the weights were below 500 gms, or whose gestational age was questionable, i.e. around 20 weeks. These cases could conceivably be eliminated from our statistical tabulation and so reduce our perinatal rate.

|                 |                     |
|-----------------|---------------------|
| Neonatal Deaths | = 42 (35 white      |
|                 | ( 7 non-white = 20% |
|                 | (15.4% in 1963)     |
| <hr/>           |                     |
| Stillbirths     | = 42 (33 white      |
|                 | ( 9 non-white = 27% |
|                 | (16% in 1963)       |

As noted, there is an increase in the non-white deaths over the previous year. This has been a trend during the past several years.

|                                |                         |   |
|--------------------------------|-------------------------|---|
| Perinatal Mortality Rate       | = 84                    | = |
| <hr/>                          |                         |   |
|                                | 2410 + 42               |   |
| <hr/>                          |                         |   |
| 84 x 1000                      | = 34.2                  |   |
| <hr/>                          |                         |   |
| 2452                           |                         |   |
| Corrected Rate                 | = 75                    | = |
| <hr/>                          |                         |   |
|                                | 2405 + 38               |   |
| <hr/>                          |                         |   |
| 75                             | = 30.7                  |   |
| <hr/>                          |                         |   |
| 2443                           |                         |   |
| <hr/>                          |                         |   |
| Perinatal Rates — past 3 years | = 27.1 — 1961           |   |
|                                | 26.2 — 1962             |   |
|                                | (corrected) 30.9 — 1963 |   |

The rate for 1964 is much the same as for 1963, but considerably greater than the two previous years. This could be explained, at least in part, by the increase in non-white deaths with their greater incidence of prematurity and poor prenatal care. When compared with the national rate of about 24/1000 our figure cannot be considered good. In the past few years, however, other cities, particularly large ones like Chicago, New York and Baltimore, have shown increasing rates rather than the reverse trend which was more common in the years preceding 1963.

Analysis Of Deaths

|                              |                         |
|------------------------------|-------------------------|
| A. Neonatal Deaths:          |                         |
| 501 — 1000 gms               | = 15 (37/42 =           |
| 1001 — 2500 gms              | = 22 ( 88% prematures   |
| over 2500 gms                | = 5                     |
| B. Fetal Deaths              |                         |
| 501 — 1000 gms               | = 12 (32/42 =           |
| 1001 — 2500 gms              | = 20 ( 76% prematures   |
| over 2500 gms                | = 10                    |
| C. Neonatal Deaths by months |                         |
|                              | J F M A M J J A S O N D |
| 501 — 1000 gms               | 1 0 2 0 0 0 2 0 2 0 5 2 |
| 1001 — 2500 gms              | 0 1 1 2 4 2 1 1 2 3 3 2 |
| over 2500 gms                | 0 0 0 0 2 0 0 0 1 0 1 1 |

#### D. Fetal Deaths by months

|                 | J | F | M | A | M | J | J | A | S | O | N | D |
|-----------------|---|---|---|---|---|---|---|---|---|---|---|---|
| 501 — 1000 gms  | 3 | 1 | 3 | 1 | 0 | 0 | 2 | 0 | 1 | 0 | 0 | 1 |
| 1001 — 2500 gms | 1 | 2 | 2 | 1 | 4 | 2 | 2 | 2 | 2 | 0 | 2 | 0 |
| over 2500 gms   | 1 | 2 | 0 | 1 | 1 | 0 | 0 | 2 | 1 | 2 | 0 | 0 |

I don't think we can draw any definite conclusions from this monthly pattern except to say that the month of November showed the largest number of neonatal deaths, with a fairly even distribution throughout the rest of the year. The fetal deaths showed very little trend from month to month. The monthly distribution of perinatal deaths is controlled for the most part by chance.

#### Causes Of Deaths

##### A. Neonatal

501-1000 gms (15) — All the results of premature separation of the placenta, cause unknown. Every one was very immature and died in a matter of minutes or hours, one only over 24 hours. RDS noted in 90%. 1 placenta previa, Pyelonephritis in one mother. In 2 cases drugs were given for first trimester bleeding (e.g. Depoprovera). 6 reported having no or insufficient prenatal care.

In this group 5 cases were considered questionable—around 500 gms or less than 20 weeks gestation.

1001 — 2500 gms (22) — 12 — Immaturity, due to premature separation and placenta previa, all showing RDS. No toxemia reported.

##### 7—Congenital Anomalies

- 1) Mongolism absence of left hand, intestinal obstruction, surgical reduction of volvulus, resection of Meckel's fecal fistula. Died in 6 hours, weight 5# 1 oz.
- 2) Polycystic kidneys, fetal atelectasis with massive hemorrhage. Weight 5# 2 oz.
- 3) Fused lower extremities, no genitalia, no anus, absence of descending and sigmoid colon and rectum. Partial atelectasis. Weight 3# 13 oz.
- 4) T.E. fistula, mongolism, no surgery performed. Given Enovid in 1st trimester for bleeding. Weight 4# 12 oz.
- 5) I A septal defect in a very immature infant with cerebral hemorrhage. Weight 3# 10 oz.
- 6) Microcephaly, no nose, cleft lip and palate, congenital heart (? Trisomy). Weight 4# 2 oz.
- 7) Achondroplastic dwarf, markedly deformed. ? congenital genetic defect. Mother had heart surgery with stormy course and was on Demerol and Digitalis. Weight 3# 9 oz.

##### 3—Erythroblastosis Fetalis

- 1) Very immature—negative titre. Weight 2# 5 oz.
- 2) Titre 1:128. Very poor condition. Hydrops, died in 15 minutes. Weight 4# 11 oz.
- 3) Titre 1:16 at 33 weeks. Died in 2 days with RDS. Weight 4# 13 oz.

##### 2—Cerebral Hemorrhage—3# 10 oz., 3# 14 oz.

##### 1—Aspiration Pneumonia—4#

##### 1—Diabetic—poor care, 3# 5 oz.

##### 1—Internal Hydrocephalus—? cause. 2# 10 oz.

As usual, considerable overlapping in the causes of death was present. Several babies had 2 or 3 causes of death (e.g. RDS & Diabetes; immaturity and congenital anomalies + RDS, etc.).

##### Over 2500 gms (5)

- 1) *Fetal pneumonia* and *HMD*. No prenatal care, 5# 14 oz.
- 2) *Separation of placenta*—cerebral hypoxia, convulsions. Poor prenatal care, weight 6# 8 oz.
- 3) *Congenital Heart Disease*. Large IV Septal defect and large DA—weight 6# 10 oz.
- 4) *Congenital Heart Disease*—Truncus, Pneumonitis as a complication. Weight 5# 11 oz.
- 5) *Diabetes*—Hypertensive mother. Caesarian Section—HMD—weight 6#.

##### B. Fetal (Stillbirths) —

##### 501-1000 gms (12)

All due to *premature separation of the placenta* but cause *unknown* in every instance. Weights varied from 12 oz. to 2# 2 oz. Four cases reported weights below 1 lb. although gestational periods were more than 20 weeks. One—due to maternal injury 2 weeks before delivery. Two due to *renal disease* in mother (one treated with Furofantin).

##### 1001-2500 gms (20) —

##### 11—Reported to be due to *incomplete separation of placenta, cause unknown*.

##### 2—Congenital Anomalies

- 1) *Tetralogy of Fallot* with large IV and I A defects. Single umbilical artery, wt. 2# 4 oz.
- 2) *Anencephaly*—weight 3 lbs.

##### 2—Intrauterine strangulation—due to cord around neck.

##### 1—Erythroblastosis Fetalis. Bad history of previous trouble. Titre 1:512. Wgt. 5# 6 oz.

##### 1—Intrauterine Anoxia—? Cong. anomalies, weight 3# 6 oz.

##### 1—Pre-eclampsia—weight 3# 12 oz.

##### 1—Fibrotic placenta. 80% fibrotic. Wgt. 5# 2 oz.



1—*Placental Insufficiency*—small placenta.  
Bleeding during 1st trimester. On Enovid,  
wt. 4# 12 oz.

over 2500 gms (10) —

3—*Premature Separation of placenta* with  
cause unknown.

2—*Asphyxia due to strangulation*. One had a  
small cord @ neck, the other torsion of  
cord.

2—*Diabetes*—placental insufficiency. Poor con-  
trol in both instances.

2—*Post Maturity*

1) One case of neglect—not seen during  
last 5 weeks. Weight 7# 6 oz.

2) Intrauterine asphyxia during labor.  
Fetal distress. Emergency C.S. Weight  
8# 10 oz.

1—*Amnionitis*. Membranes ruptured for sev-  
eral days. Weight 7# 12 oz.

### Preventable Or Avoidable Deaths

A. *Inadequate or no Prenatal Care* (13) =  
15.4% of the total perinatal deaths. A large pro-  
portion of these are non-whites or whites in the  
low income class. This group from year to year  
consistently contributes the largest number to our  
preventable deaths.

B. *Others*

1) Mother a known *diabetic* since 5 years of  
age with 3 previous abortions. Very poorly  
controlled. Weight 3# 5 oz. With more  
careful control of her diabetes the baby  
might have been saved.

2) *Maternal injury* 2 weeks before spontane-  
ous labor (kicked by a horse). This infant  
might have gone on to term and survived  
without the accident. Weight 12 oz.

3) *Postmature infant*—44 weeks. Mother neg-  
lected to see her doctor during the last 5  
weeks. If she had sought proper care, this  
infant might have lived. Weight 7# 6 oz.

4) *Amnionitis* in a mother whose membranes  
were ruptured for several days. Weight  
7# 2 oz.

5) Overweight *diabetic* mother (270 lbs) with  
poor diabetic control. Weight 7# 5 oz.

6) *Postmature* patient (42½ weeks). Intra-  
uterine asphyxia. Emergency Caesarian  
section during labor because of fetal dis-  
tress. The question of not seeking a con-  
sultation for a primipara in labor over 12  
hours is raised.

The total preventable or questionably prevent-  
able deaths = 19 (22.6% of the total perinatal  
deaths). This percent hasn't changed much in the  
last 3 years, (20% in 1962 and 21% in 1963) but  
a slight rise is noticeable.

AUTOPSIES: (newborns = 27 (64%)  
(stillborns = 15 (36%))

### Leading Causes Of Death

|                                                                                                                                                   |       | Average |
|---------------------------------------------------------------------------------------------------------------------------------------------------|-------|---------|
| Immaturity                                                                                                                                        | 32%   | 37%     |
| R D S                                                                                                                                             | 41.7% | 26%     |
| Congenital Anomalies                                                                                                                              | 15.5% | 12%     |
| Birth Injuries                                                                                                                                    | 3.6%  | 10%     |
| Others (Includes E.F. (4), Dia-<br>betes (2), Aspirations (1), In-<br>fections (4), Postmaturity (2),<br>Cord Strangulation (2), Toxe-<br>mia (2) | 7.2%  | 8%      |

### Conclusions:

1) Prematurity remains the single most impor-  
tant factor in perinatal mortality. In our hospital,  
the premature rates seem to be increasing from  
year to year, with 88% neonatal deaths and 76%  
fetal deaths in this category during the past year.

2) R D S (Respiratory Distress Syndrome) seems  
to be on the increase. This could possibly be due  
to our higher rate of prematures.

3) The most significant changes are noted in the  
rising number of deaths due to congenital anoma-  
lies, and a decrease in those due to birth injuries.  
This may indicate an improvement in our Obstet-  
rics, but factors responsible for the increase in  
anomalies still remain obscure, particularly factors  
that might play a role in the 1st trimester, i.e.  
maternal infections and ? medications.

4) Poor prenatal care continues to be a most  
important factor, occurring in about 15% of our  
perinatal deaths, and showing no improvement  
from year to year. This situation prevails about  
twice as many times in non-whites as in whites.

5) Our perinatal death rates show evidence of  
not improving. In fact, during the last two years  
it has increased rather than fallen. We do not feel  
that this is due to inferior Obstetrics or Pediatrics,  
but it is possibly due to an increase in the num-  
ber of non-white and low income patients coming  
to this hospital. We consider Obstetrics and Pedi-  
atrics, as practiced in HSR, of high calibre.

### Recommendations

1) Improved education and facilities to handle  
our low income families more adequately. Perhaps  
community prenatal clinics could be set up to help  
those who have difficulty in getting to our hos-  
pital clinic. In this way fewer patients would be  
in the "poor prenatal care" category, and as a con-  
sequence the prematurity rate would fall.

2) More careful evaluation of the newer meth-  
ods of treating R D S, and the possible adoption of  
a proven technique such as the use of IV glucose

and bicarbonate based on PH studies, as recommended by Smith, Usher, and others. Good laboratory co-operation is essential. A lab set-up and portable x-ray unit might be considered for the Pediatric newborn area.

3) More intensive study and research of factors that might play a role in the formation of anomalies, particularly drugs and infections in early pregnancy. A research lab in the department of Obstetrics should be considered.

4) Development of newer techniques in the prenatal study and treatment of erythroblastosis fetalis. Exciting developments in the past year or so have led to great advances in this field, with more and more formerly hopeless infants being saved. Amniocentesis with chemical and spectrophotometric methods of measuring bilirubin content can help determine very accurately the optimum time to induce labor and to give fetal transfusions. Close

co-operation between the Obstetric and Pediatric Departments is imperative to obtain the best results.

5) Reference is made to the various local state and federal agencies that are interested in preventing fetal loss, such as the Polio Foundation, Associations for the Retarded, Cerebral Palsy, N.I.H., etc. Considerable research is now being directed toward this field.

Respectfully submitted,

WILLIAM GLASER, M.D., *Chairman,*  
Perinatal and Morbidity Committee.

Perinatal and Morbidity Members:

William Glaser, M.D., Chairman  
Robert Nesbit, M.D.  
Michael Lavorgna, M.D.  
Bernard Swan, M.D.  
Norton Kazanjian, M.D.

# SAVE THE DATE

**NOVEMBER 16, 1966**

*for*

**One-Day Seminar On Perinatal Problems**

**Mary Harkness Auditorium — Cedar Street, New Haven**

Speakers include: Arthur J. Lesser, M.D., Deputy Chief, Children's Bureau, Welfare Administration, Department of Health, Education and Welfare; Robert E. Cooke, M.D., Chairman, Department of Pediatrics, Johns Hopkins University, School of Medicine; Robert E. L. Nesbitt, Jr., M.D., Chairman, Department of Obstetrics and Gynecology, State University of New York, Upstate Medical Center, Syracuse; and Sydney Gellis, M.D., Professor, Department of Pediatrics, Tufts University, College of Medicine.

Sponsored by: Connecticut State Medical Society's Committee on Perinatal Morbidity and Mortality, Department of Pediatrics, Yale University School of Medicine, and Connecticut State Department of Health.



## **IMPORTANT — PLEASE READ**

### **TUMOR REGISTRY REPORTING**

At the Council meeting of July 14, 1966, a resolution concerning the Tumor Registry (published below) was adopted. The purpose of the resolution is to remind practitioners of the importance of continuing to cooperate fully with their hospital registries, as they have in the past, and to emphasize the growing importance of making follow-up reports to those same registries on cases in which therapy is administered primarily in the doctor's office or other outpatient facility.

**WHEREAS:** The medical profession of Connecticut, through the Connecticut State Medical Society, was responsible for the passing of the bill establishing the Connecticut Tumor Registry in the State Health Department, and

**WHEREAS:** The physicians have always cooperated with their respective hospital registries in reporting and following all cases of cancer diagnosed in Connecticut, and

**WHEREAS:** The members of the medical profession voluntarily have continued to support this activity which has resulted in the better quality of the information submitted to the Central Registry, therefore bringing about better diagnoses and treatment of the cancer in Connecticut, and

**WHEREAS:** The data thus collected in the registries have been and continues to be used by the physicians of the state, the nation, and internationally in the analysis and interpretation of all phases of the cancer problem, therefore be it

**RESOLVED:** That the Council of the Connecticut State Medical Society urge the physicians of Connecticut to continue their cooperation with the State Health Department and the Central Tumor Registry by working together with the hospital registries in completing requests for follow-up information, and be it further

**RESOLVED:** That the Council also urge that all subsequent treatment known to the physician, with special emphasis on x-ray and drug therapy administered on an out-of-hospital basis, be brought to the attention of the hospital registry secretary by the treating physician.

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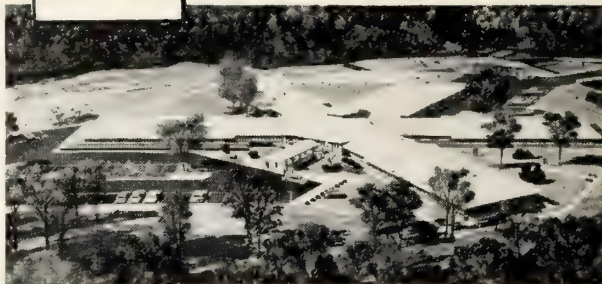
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## NOTICE OF SPECIAL REPORT\*

*For many years, the State Health Department and other agencies have been using as a guide to evaluating obstetrical departments in Connecticut a document titled: "Recommended Standards for Obstetrical Care." On May 25, 1966, the Council accepted a report filed by the Society's Committee to Study Maternal Morbidity and Mortality which revised that section of the document titled: "Prevention and Treatment of Toxemias of Pregnancy"; authorized publication of the report in CONNECTICUT MEDICINE; and approved its transmittal to the State Department of Health and the chiefs of community hospital obstetrical services to be used voluntarily as a guide to evaluating the structure and function of such services.*

## REPORT OF THE COMMITTEE ON MATERNAL MORBIDITY AND MORTALITY OF THE CONNECTICUT STATE MEDICAL SOCIETY

### Subject: Recommendations For The Prevention And Treatment Of Toxemias Of Pregnancy

#### Prenatal Routine

#### I. Prophylaxis

A. Frequency of patient's visits to physician through prenatal course.

1. A minimum of one visit every four weeks up to 28 weeks.
2. A minimum of one visit every two weeks from 28 to 36 weeks.
3. A minimum of one visit every week from 36 weeks to delivery.

#### B. Content of first visit.

1. Complete history and physical examination.
2. Complete urinalysis.
3. Blood group and Rh determination.
4. Instruction as to diet and weight control.

#### C. Content of each subsequent visit.

Each visit should include as minimum:

1. The recording of blood pressure and weight.
2. The testing of urine for albumin and sugar.
3. The questioning of patient regarding symptoms of edema, headache, epigastric pain, blurring of vision.
4. Instructions as to diet. Sodium restriction (eliminating salty foods, table salt, and baking soda), high protein, high mineral high vitamin.
5. Check on weight control—gain of no more than two pounds per month. Total weight gain of no more than 20 pounds over ideal weight.

6. Special attention given to abnormalities. More frequent visits for patients with essential hypertension, diabetes, urinary disease and previous toxemias. Obstetrical consultation is desirable in such cases because of their tendency to develop toxemia.

#### II. Management of the office patient who shows:

##### A. Excessive weight gain.

1. Diet, low sodium, high protein, mineral and vitamin. Have patient tabulate diet for one week and submit the same. Diuretics may be considered.
2. More frequent visits.
3. Hospitalization if uncontrolled.

##### B. Hypertension.

1. Blood pressure 140/90 or over, or rise of diastolic of 10 or more, or a systolic of 20 or more.
2. Check urine for infection (culture clean catch specimen).
3. Diet, low sodium and high protein.
4. More frequent visits.
5. Rest at home.
6. Sedation.
7. Report headache, edema, epigastric pain or blurring of vision at once.
8. Hospitalization if not controlled.
9. If in doubt, have obstetrical consultation prior to admission.

##### C. Edema of face, hands or feet.

Treatment same as for excessive weight gain.

##### D. Albuminuria.

Treatment same as for hypertension.

\* This identification was inadvertently omitted in the July issue.

- E. Hospitalization should be urged if:
1. In spite of good conservative treatment weight continues to increase excessively.
  2. Elevated blood pressure continues (140/90) or blood pressure continues to rise in spite of good conservative treatment as outlined.
  3. Persistent edema together with unusual weight gain.
  4. Albuminuria continues to be present or is increasing in amount.
- F. Patients reporting any of the following symptoms *should be seen immediately*:
1. Severe headache.
  2. Sudden edema, particularly of the face.
  3. Epigastric pain.
  4. Blurring of vision.
- G. Immediate hospitalization if there is:
1. Sudden rise in blood pressure (such as 160/100).
  2. Evaluate other symptoms and if due to toxemia, admit.
  3. Convulsion.

H. Early hospitalization of toxic patient is of paramount importance in preventing more severe or even fatal progress of this disease.

#### **In-Hospital Procedures**

Upon admission to hospital toxemia routine should be started and consultation rules adopted by the hospital should be adhered to. It is strongly recommended that wherever toxemia patients are being treated, a special toxemia tray containing necessary emergency drugs and IV solutions be readily available.

- A. If patient is pre-eclamptic upon admission to hospital:
1. Treat conservatively for 24-48 hours or longer.
  2. If patient is not near term and good results are being obtained from conservative treatment, ideally continue hospitalization. If patient becomes sufficiently improved, patient may be seen in doctor's office at least twice a week. Treat conservatively until baby is viable or as long as possible. If it is apparent that conservative treatment is failing, re-hospitalize patient.
  3. Toxic patients must be seen frequently by nurses and doctors.
  4. If patient is at or near term, consider delivery:
    - (a) Whether multipara or primigravida, induce if possible.
    - (b) If induction in either case seems impossible or is unsuccessful, Caesarean section should be considered.

- B. Toxemia with convulsions (eclampsia) should be treated conservatively until controlled. Then deliver by the most feasible method. Avoid Caesarean section if possible. Consider induction by oxytocin drip and rupture of membranes.

#### **Toxemia Routine For Hospitalized Maternity Patients**

1. Consultation recommended.
2. Single bedroom if possible and no visitors.
3. Complete bed rest.
4. Weigh patient on admission and daily.
5. Record intake and output.
6. Low sodium, high protein diet.
7. Blood pressure, temperature, pulse, respirations, and fetal heartbeat every four hours.
8. Clean catch urine on admission for routine analysis and culture; daily clean urine thereafter for routine analysis.
9. Blood chemistries
  - (a) Draw blood on admission for BUN, Creatinine, uric acid, total serum protein, CO<sub>2</sub> combining power, sodium, potassium chlorides and blood sugar.
  - (b) Repeat chemistries as indicated.
10. Hematocrit and hemoglobin on admission.
11. Sedation.
12. At least one 24 hour urine for total protein if 3+ or 4+ albuminuria is present.

#### **Important**

It must be clearly understood that no routine will cover all pre-eclamptic patients. The above routine is merely intended as a guide. It will be modified for the patient who is responding satisfactorily—and will be changed somewhat for the patient who is not improving—and, of course, must be modified drastically for the patient who is a severe toxemia with imminent convulsions or has already convulsed. It is most important (a) that the toxic patient both before and after delivery be watched carefully even though she may appear to be improving (her condition may change quickly); (b) that a competent consultant accept the responsibility for the patient's care.

#### **Postpartum Toxemia Routine**

It is assumed that there are routine postpartum orders in each hospital licensed by the Connecticut State Department of Health to take care of obstetrical patients.

Treatment of the postpartum toxic patient cannot be made a routine except in principle. The first forty-eight hours postpartum, and particularly the first eight hours, are the most critical.



It must be remembered that in the care of postpartum toxemia, pre-eclampsia or eclampsia that (1) it may develop for the first time postpartum, (2) pre-eclampsia may be made more severe by labor or may progress into eclampsia. With this in mind, the following recommendations are made.

- I. Urine.
  - A. Test urine taken at time of delivery for albumin immediately.
  - B. Examine subsequent urines for albumin daily if signs of toxemia persist.
  - C. Obtain clean catch urine on the third day postpartum for urinalysis and culture (in order to detect pyelonephritis).
- II. Blood Pressure.
  - Take and record blood pressure:
  - A. Immediately following delivery.
  - B. Then every half hour for two hours.
  - C. Then every one to two hours for six hours.
  - D. Then q.i.d. until discharged.
- III. Medication.
  - A. Continue medication postpartum under consultant's orders.
- IV. Activity.
  - A. Continue with complete bed rest until patient is ordered up by physician.
- V. Intake and output.
  - A. Record intake and output until discontinued by physician.
- VI. Blood chemistries—repeat as indicated.
- VII. Diet.
  - A. Continue low sodium diet postpartum until signs of toxemia have disappeared.
- VIII. Hospitalization.
  - A. Extend usual hospital stay as indicated.

---

## Early Days Of Frozen Foods

John Gorrie, an American, is credited with having invented in 1849 a cold-air refrigerating machine such as was used there in the early stages of the frozen-meat trade. Patents for producing cold and making ice, either by expansion of compressed air or by the evaporation of volatile liquids, began to follow one another at fairly frequent intervals in the 1850s, and probably the first refrigerating plant to be applied to a manufacturing process (in a paraffin factory) was due to James Harrison—who improved upon the Perkins machine. Harrison was a native of Glasgow but emigrated to Australia in 1837. He became editor of the "Melbourne Age" and is reported to have been the first to see the "enormous source of wealth that lies still undeveloped in the export of meat from the Australian pastures." It will be remembered that Australia was the first country to export canned meat. Harrison interested himself in refrigeration and erected an ice-factory at Rodey Point in Victoria at a cost of £1000. In 1851 he installed a refrigerating machine for a brewing firm at Bendigo, which was the world's prototype of such machines. Later, Harrison devoted himself to meat-freezing and, at Melbourne in 1873, several carcasses of sheep, sides of beef, poultry, and fish, which he had kept frozen for six months, were consumed at a public banquet.—Morris, T. N.: "Management and Preservation of Food," in Singer, C., et al (eds.): *A History of Technology*, vol. 5, Oxford: Clarendon Press, 1958, pp. 46-47.

## Special Notice

### OCCUPATIONAL MEDICINE

A special course in occupational medicine will be offered by the Yale School of Medicine, Department of Epidemiology and Public Health, during the fall term. Professor Richard Schilling, Head of the Department of Occupational Health and Applied Physiology of the London School of Hygiene and Tropical Medicine, will be in New Haven during that period. He and Dr. Arend Bouhuys of the Pierce Foundation will assist Dr. J. Wister Meigs, Associate Professor of Epidemiology (Occupational Medicine) in teaching the course. It will consist of a combination of field trips to selected industries, class discussions and epidemiological assignments. The schedule will involve 2 classes a week of approximately 2 hours each, although field trips may require up to 3 hours. The course is open to physicians without charge. Further information may be obtained from J. Wister Meigs, M.D., Room 407, 60 College Street, New Haven, Connecticut. 06510.

Date and time to be announced.

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## Letter To The Editor

Dear Dr. Nahum:

This is a belated tribute to you for an excellent editorial in the September 1965 issue of *Connecticut Medicine*. The title is "Who is Suggestible?" and it is sound and sensible. Further, I've never encountered this particular attitude and explanation in my reading elsewhere.

Now, at 81, I do little hypnosis but I'm sure I will have occasion to keep your thoughts in mind.

DANIEL P. GRIFFIN, M.D.

Bridgeport, Connecticut

*Letters to the Editor are welcome and will be published for informative and educational purposes as space permits. As with other material which is submitted for publication, all letters will be subject to the usual editing. Address all correspondence to: THE EDITOR, CONNECTICUT MEDICINE, 160 St. Ronan Street, New Haven, Connecticut, 06511.*

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## Around The State

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### CONNECTICUT MEDICAL PRESS AWARDS



Dr. Orvan W. Hess (right), Society President, presents the 1966 Connecticut Medical Press Award for feature writing to Ned Thomas of the New Haven Sunday Register. In the center is Robert J. Leeney, Executive Editor of the Register.



The Hartford Times captured two awards in the 1966 Connecticut Medical Press Awards competition. Council Chairman Dr. Stevens J. Martin (left) presents plaque and \$150 check to Ivan Robinson (center), winner of the news reporting category, and E. Malcolm Stannard, who took honors for editorial writing.

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Three veteran newsmen have been presented the 1966 Connecticut Medical Press Awards of the Connecticut State Medical Society.

The winners are: E. Malcolm Stannard, Editorial Page Director of the Hartford Times; Ned Thomas, Feature Writer, New Haven Sunday Register; and Ivan Robinson, News Reporter, Hartford Times.

The award-recipients were each given a \$150 check by Dr. Orvan W. Hess, Society President, and Dr. Stevens J. Martin, Council Chairman. They also received bronze plaques.

The editorial writing citation presented to Stannard stated: "His grasp of the dominant role played by socio-economic problems in the life of our nation and his knowledgeable discussion of these problems constitute a real public service."

Thomas, who received the feature writing award, was cited for his six-part series on progress in medicine which "offered the lay reader a highly readable presentation of the new techniques and drugs being employed to curb and possibly cure man's principal killers; it is one of the most comprehensive medical series seen in Connecticut newspapers."

The citation presented to Robinson in the news reporting category stated: "His knowledge and subject matter are wide-ranging, covering diverse aspects of pure medicine as well as socio-medical problems; he has the professional writer's control of his subject, and his articles are crisply and tightly written."

The Judging Committee was headed by Dr. Luca E. H. Celentano, chairman of the Public Relations Division.

## The Connecticut Hospital Association Annual Meeting



Officers of the Connecticut Hospital Association are, from the left: Edmund S. Wolfe, a trustee of Bridgeport Hospital, treasurer; T. Stewart Hamilton, executive director of Hartford Hospital, newly-elected president; Lewis E. Caplan, retiring president; and Philip A. Coleman, a trustee of Bristol Hospital, president-elect. Hamilton is a former president of the American Hospital Association.

T. Stewart Hamilton, M.D., executive director of Hartford Hospital, was elected president of the Connecticut Hospital Association at the organization's recent annual meeting. He succeeds Lewis E. Caplan of New Haven.

Dr. Hamilton is a former president of the American Hospital Association.

Other new officers are: Philip A. Coleman, a trustee of Bristol Hospital, president-elect; and Edmund S. Wolfe, a trustee of Bridgeport Hospital, treasurer.

A high point of the meeting was a report by Arthur Rogers of Waterbury on progress of the newly-formed Hospital Planning Commission, a coordinating body for hospitals and related health facilities.

The principal speaker, John H. Knowles, M.D., general director of Massachusetts General Hospital, discussed "Experts, Enclaves and the Public Interest."

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## News From Yale University School Of Medicine

The Yale School of Medicine and the University of Connecticut School of Medicine will head one of the nation's five pioneer planning projects under the new federally-sponsored program to combat heart disease, cancer, stroke, and related diseases.

The National Institutes of Health announced an award of \$759,000 for joint planning by the two medical schools.

In a statement, Dean Vernon W. Lippard of the Yale School of Medicine and Dean John W. Patterson of the University of Connecticut School of Medicine said that "the grant places the Connecticut region in the forefront of the planning phase of this unprecedented effort to develop regional medical programs for improving the health of the people."

The purpose of the grant is to finance a two-year program of studies and planning for a future co-operative network in Connecticut among the medical schools, physicians, community hospitals, and voluntary health organizations for research, education, and related demonstrations of patient care.

Implementation of the planning program will begin this July 1, according to Robert P. Lawton, Associate Dean of the Yale School of Medicine, who is program coordinator for administering the grant. An initial step will be the recruitment of a professional staff, including a planning director, as well as research assistants and clerical personnel.

### 1966 MEETINGS

**September 28** — 41st Connecticut Clinical Congress to be held at Mary S. Harkness Auditorium, Yale University Medical School, New Haven, Connecticut. The program will be devoted to "Recent Advances in the Diagnosis and Management of Liver Disease" and "Recent Advances in the Diagnosis and Management of Thrombophlebitis."

**September 29-30**—Seminar on Diabetes. Deauville Hotel, Miami Beach, Florida. G. F. Cahill, S. S. Fajans, W. J. Harrington, A. G. Hills, E. C. Miller, M. Siperstein, W. C. Thomas, will be guest speakers. Florida Diabetes Association, R. T. Rengarts, M.D., Secretary, P.O. Box 268, Sebring, Florida 33870.



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## Woman's Auxiliary To The American Medical Association — June 26-30, 1966 Chicago, Illinois

### Capsule Report

Connecticut's Mrs. Norman Gardner, former State Auxiliary President was elected as one of the 10 new directors of the National Auxiliary Board at the Convention. Betty also gave an excellent report as the Retiring Chairman of the National Rural Health Committee.

Mrs. William Richards, your immediate past president was first on the podium with her knowing report on the Connecticut State Auxiliary's Projects and Programs for the year 1965-1966.

Freddie worked many long hours as a member of the Election Committee for the National Auxiliary during the Convention.

Connecticut's Delegates to the convention were: Mrs. John D. O'Connell, Presidential Delegate; Mrs. William R. Richards, Delegate; Mrs. Max Caplan, Delegate; Mrs. F. Erwin Tracy, Delegate; Mrs. Edwin R. Connors, Delegate.

Bylaws, amendments providing major structure revision, a new high in AMA-ERF contributions

and an open forum for state presidents and presidents-elect were outstanding features of the convention.

In her inaugural address, Mrs. Asher Yaguda, the National President, urged auxiliaries to escalate their leadership roles in voluntary service and to reassess the auxiliary program plan, stressing health programs for all age groups.

Confusion of interpretation, Profusion of Medical Services and Infusion of huge sums of Federal Monies seemed to be the status of Medicare as discussed at the convention.

MRS. ANTHONY CIPRIANO

### Dates To Remember

Board Meetings—Sept. 19, Oct. 17, Jan. 16, 1967, March 20, 1967. Semi-Annual Meeting—Nov. 14 or 15. Annual Meeting—April 26, 1967.

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## Doctor's Office

Anthony P. Borelli, M.D., announces the opening of an office for the practice of obstetrics and gynecology on the Newtown-Danbury Road, Newtown.

Matthew P. Campione, M.D., announces his association in the practice of general surgery with Dr. Donald H. Badner and Dr. Alfred T. St. James at 405 Broad Street, Meriden.

Norman M. Canter, M.D., announces his association with Dr. Andrew Owens in the practice of general surgery at 50 Ridgefield Avenue, Bridgeport, and 325 Reef Road, Fairfield.

William M. Edmonstone, M.D., Richard M. Barry, M.D., and L. Edwin Sproul, M.D., announce the removal of their office in Mystic to Sandy Hallow Road in that city. Their New London office will remain at 464 Ocean Avenue, New London.

Adolph Franz, M.D., announces his association with Drs. George Fox, T. C. Flynn and Francis Tonkonow, in the practice of orthopedic surgery at 147 West Main Street, Meriden.

Robert J. Kerin, M.D., announces his association in the practice of orthopedic surgery with Dr. Michael McLoughlin of Boston, Massachusetts and Dr. Earl E. VanDerwerker of Hartford at 112 Broad Street, Milford.

Harry R. Kormos, M.D., announces the removal of his office for the practice of psychiatry to 34 Imperial Avenue, Westport.

John A. Muccino, M.D., announces the opening of an office for the practice of obstetrics and gynecology at 21 Woodland Street, Hartford.

Michael R. Sharon, M.D., announces the opening of an office for the practice of internal medicine and cardiology at 57 Union Street, Rockville.

Frank E. Smith, Jr., M.D., announces the association of Peter H. Gott, M.D., with him in the practice of medicine in Lakeville and at the Canaan Savings Bank Building in Canaan.

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## OBITUARY

### Alfred Schiavetti, M.D. 1905 - 1966

Dr. Alfred Schiavetti died less than twenty-four hours after suffering a heart attack on April 14, 1966.

He was born in Newark, New Jersey, attended Columbia University and received his M.D. from Tufts University School of Medicine in 1930. After serving his internship at St. Mary's Hospital in Hoboken, a residency at the Jersey City Medical Center and one at Manchester Memorial Hospital, Manchester, Connecticut, he set up practice in Stamford Springs, Connecticut in 1935.

He was for many years chief of staff and chief of surgery at the Johnson Memorial Hospital. He also served as Corporator and a member of the Board of Trustees at Johnson Memorial Hospital.

He was a member of the Connecticut State Medical Society, Tolland County Medical Association, American Medical Association and the American Society of Abdominal Surgery.

He is survived by his wife, Betty, three children, Dreda, Alfred, Jr., and Nicholas and one granddaughter.

His untimely death has been a great loss to the community where he was for so long a respected citizen and physician-surgeon.

ALBERT M. DETORA, M.D.

### COURSE IN POSTGRADUATE GASTROENTEROLOGY

October 27, 28 and 29, 1966

The Annual Course in Postgraduate Gastroenterology of the American College of Gastroenterology will be given at the Bellevue Stratford in Philadelphia, Pennsylvania, 27, 28, 29 October 1966.

The moderators for the course will again be Dr. I. Snapper, Consultant, Ft. Hamilton Veterans Administration Hospital, Brooklyn, N.Y. and Dr. John L. Madden, Clinical Professor of Surgery, New York Medical College and Director of Surgery, St. Clare's Hospital, New York, N.Y.

The faculty for the course will be drawn from the Medical Schools in and around Philadelphia. The subject matter to be covered, from the medical as well as the surgical viewpoint, will be essentially, the diagnosis and treatment of gastrointestinal diseases and comprehensive discussions of diseases of the esophagus, stomach, pancreas, liver and gallbladder, small intestine and colon. A session on instrument technics will be held at the Albert Einstein Medical Center, Northern Division.

For further information and enrollment, write to the American College of Gastroenterology, 33 West 60th Street, New York, N.Y. 10023.



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## NEW BOOKS IN REVIEW

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**PEDIATRIC ELECTROCARDIOGRAPHY. Normal and Abnormal Patterns, Incorporating the Vector Approach.** Warren G. Guntheroth, M.D. The W. B. Saunders Co., Philadelphia and London, 1965. 150 pp. with 108 figures. \$7.00.

Reviewed by: LOUIS H. NAHUM

This little book fully realizes the authors stated purpose to provide an accurate but brief introduction to an approach to electrocardiography. Being himself a pediatrician, the emphasis is on pediatric experience but this is only incidental. Practically every scalar electrocardiogram is accompanied by a vectorcardiogram which should not be taken too seriously because there is no theoretical vector, and we now know that there are wide divergencies between a calculated dipole and the axis of the observed bipolar distribution of the surface field function. Furthermore from the students point of view of electrocardiogram is less formidable and its modifications now rest on a firm experimental basis.

The author exposes the fallacy of the unipolar concept. However certain other assumptions such as transmission of impulse perpendicularly from endocardium to epicardium are assumed to be true. This does not affect the interpretation of the given records however. The concept of cancellation of current is well stated but this could have led the author to use this principle to explain the electrical silence of subendocardial layer of the myocardium and the reason for the preponderance of potentials derived from the surface layers of both the right and left ventricle in the production of the surface field function.

This book however is lucidly written and excellently illustrated by the author's drawings and should assist a beginner to enter the field in electrocardiography provided he realizes that the experimental basis for electrocardiography must be observed elsewhere.

**EFFECTIVE PSYCHOTHERAPY, A Contribution of Hellmuth Kaiser, Edited by Louis B. Fierman, M.D. Foreword by Allen J. Enelow, M.D. and Leta McKinney Adler, Ph.D. The Free Press, New York, 1965. xxvi, 217 pp.**

Review by: LEO H. BERMAN

Science often becomes excessively structured and solidified, and this is even more true of art. Psychotherapy, which is both a science and an art, is therefore particularly subject to the freezing into molds and conversely the establishment of dissident groups. In no other area of medicine today is there such a variety of "schools", as in psychiatry, where one can find Freudian, Sullivanian, Horney, Cultural, Organic, Behavioral, and numerous other factions. It may be difficult for physicians in other specialties to understand why there should be such strong feelings which are revealed when orthodox Freudian views are challenged. It is apparently very disquieting and unstabilizing to have basic precepts

questioned, particularly when one has struggled for some time to put down the questions and uncertainties which have arisen during the training period and particularly during the years of practice.

How doubts and conflicts can be utilized in a healthy and constructive manner is demonstrated in a new book, "Effective Psychotherapy, The Contribution of Hellmuth Kaiser", edited by Louis B. Fierman, M.D., who is chief of the psychiatric service of the West Haven Veterans Administration in Connecticut, and Associate Clinical Professor Psychiatry, Yale University, School of Medicine. This engrossing book contains the sum total of the writings in English of Hellmuth Kaiser, who for a period of time, practiced as an analyst in Hartford. The three papers here collected, are both entertaining and informative on a number of levels, serving most of all to permit the reader to have a look into the mind of an analyst struggling with the problems of how best he could understand and treat his patients.

In the first essay, "The Problem of Responsibility in Psychotherapy", published in 1955, Dr. Kaiser strongly emphasized his view that the outcome of therapy is what the therapist and not what the patient does. This is at first startling to comprehend, but when its full meaning becomes clear, it is as if a whole new frontier has been opened up. The therapist is not permitted the luxury of an escape hatch in such formulations as, "the patient is too resistant", or "she did not really want to get well." Instead, the therapist is forced back to reconsider why he is unable to establish a meaningful communication with the patient. In discussing this problem, Kaiser focused on the problems of the discrepancy between what the patient says and what he means. This discrepancy, or duplicity, became a nuclear problem which concerned him for the remainder of his life.

The way he viewed this problem and why he placed so much importance upon it is developmentally described in the second essay in the book. This, "The Universal Symptom of the Psychoneurosis, a Search for the Condition of Effective Psychotherapy" is written in the form of a novel depicting the growth and genesis of the ideas of an ever-searching psychoanalyst. It is as if Kaiser invited one along on a long sight-seeing trip with many excursions, of his own internal edifice, pointing here to doubt, there to a conclusion, here to a contradiction, there to a resolution. Many others must have had similar doubts, but few were as courageous in acknowledging them in attempting to use them for stepping stones for new techniques in therapy.

In this hitherto unpublished work, Kaiser proposed the view that the duplicity in communication, noted before, is a universal symptom. Furthermore, this he concludes is an expression of a universal conflict from the attempt of the patient to merge with or fuse with another. Furthermore, he concluded that effective therapy consisted merely of establishing meaningful, direct, and honest communications with the patient, which eventually leads the patient to acceptance of his separateness.

This novella was unfortunately left incomplete, but was illustrated by the third paper in the book, "Emergency - Seven Dialogues Reflecting the Essence of Psychotherapy in an Extreme Adventure," which tells of a therapist who is approached by the wife of a psychiatrist to treat her husband without his knowing that he is under treatment. This is possible because Kaiser believed that all that was required for treatment was that the therapist meet the patient regularly for a sufficient period of time. Actually no conditions need be set, no instructions given.

The three slim essays serve but to whet the appetite. One lays down the book with regret that Kaiser did not have an opportunity to develop his ideas further, and to write more about them. One must particularly regret that Kaiser did not have enough of an opportunity to exchange his ideas with others to permit a cross-fertilization and interaction. In some instances his views sound strange and radical, while at other times one can see linkages to the existentialists or to others who departed from orthodox views, such as Franz Alexander or Bernard S. Robbins.

Reduction to a universal symptom or to a universal conflict may be over-simplification. Though Kaiser hints at the corrective value of mutual and cooperative activity, he did not have the opportunity to develop this adequately. There are many ideas that need nurturing and further growth. The tragedy would be if this work was to be dismissed because the views were too far from orthodoxy. Walter Nigg, in his book, "The Heretics", wrote "(Heretics) do not think in collective or authoritarian categories. They examine things independently, intrepidly, and are wholly free of the widespread but pernicious tendency to be always joining the majority. They are people who subscribe to the seldom obeyed words of the Bible, You shall not follow a multitude. Among the heresies which must be said about "The Heretics" is this: The heretics were truly creative people who produced new and imperishable religious ideas. In spite of the initial vexations which are inevitably connected with new ideas, Christianity cannot do without them." We must be grateful to Dr. Fierman for bringing to our attention the exciting heresies of Dr. Kaiser.

**THE BURN WOUND.** by Stanley E. Order, M.D. and Colonel John A. Moncrief, M.D., The Charles C. Thomas Co., Springfield, Illinois, 1965. 72 pp. Illustrated. \$7.75.

Reviewed by: JAMES R. CULLEN

The publisher states that this is "a well-illustrated monograph reviewing the dynamics of the burn wound and its relationship to clinical management," and after reading the book one will readily agree with this statement.

An excellent introduction gives a brief history of the treatment of burns during the past fifty years with emphasis on the high incidence of burns in recent years and the morbidity and mortality associated with them in this country.

The subject matter deals essentially with experimental and clinical manifestations of second and third degree burn wounds; discusses sepsis due to progressive bacterial invasion associated with all burns; and has a chapter on *Pseudomonas Aeruginosa*, a very common bacterial pathogen, by William A. Shucart. This is followed by a chapter on clinical *Pseudomonas* burn wound sepsis.

Following the material on experimental burns, the authors discuss proper therapeutic approaches to the burn wound based on their experimental findings. They review at some length topical chemotherapy and the use of homo- and heterografts.

The conclusions from their work stress the need for thorough examination of the burn wound and the use of proper topical chemotherapy with the necessity for a continuing search for other local agents. In larger burn areas of 60 per cent or greater in which third degree burns predominate, the use of homograft or autograft is essential for survival.

This book is easily read and I believe should be in the possession of all physicians treating burn wounds.

## BOOKS RECEIVED

*Books received for review are acknowledged in this department and such acknowledgement must be regarded as a sufficient return for the courtesy of the sender. Selection will be made for review in the interests of our readers and as space permits.*

*Heritable Disorders Of Connective Tissue.* 3rd Edition. Victor A. McKusick, M.D. The C. V. Mosby Co., St. Louis, Missouri, 1966. 499 pp. with 190 illustrations and two in color. \$18.50

*Current Diagnosis.* A Biennial Volume of Clinical Diagnostic Methods and Evaluations. Edited by: Howard F. Conn, M.D., Robert J. Clohecy, M.D. and Rex B. Conn, Jr., M.D. W. B. Saunders Co., Philadelphia and London, 1966. 843 pp. Illustrated. \$19.00.

*Diseases of the Heart.* Third Edition. Author: Charles K. Friedberg, M.D. The W. B. Saunders Co., Philadelphia and London, 1966. 1787 pp. Illustrated. Price: Single Volume—1787 pp. \$22.00; Two-Volume Set—pp. 1-930, pp. 431-1787 \$26.00.

## CHANGES OF ADDRESS

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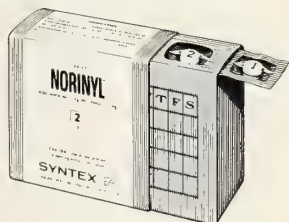
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firm the findings of the Ad Hoc Advisory Committee appointed by the Food and Drug Administration to review this possibility. Cardiac, renal or hepatic dysfunction. Carcinoma of the breast or genital tract. Patients with a history of psychic depression should be carefully studied and the drug discontinued if depression recurs to marked degree. Patients with a history of cerebral vascular accident.

**Warning:** Discontinue medication pending examination if there is sudden partial or complete loss of vision, or if there is a sudden onset of proptosis, diplopia or migraine. If examination reveals papilledema or retinal vascular lesions, medication should be withdrawn.

**Precautions:** By May 1963, experience with norethindrone 2 mg.—mestranol 0.1 mg. had extended over 24 months. Through miscalculation, omission or error in taking the recommended dosage of Norinyl, pregnancy may result. If regular menses fail to appear and treatment schedule has not been adhered to, or if patient misses two menstrual periods, possibility of pregnancy should be resolved before resuming Norinyl. If pregnancy is established, Norinyl should be discontinued during period of gestation since virilization of the female fetus has been reported with oral use of progestational agents or estrogen. When lactation is desired, withhold Norinyl until nursing needs are established. Existing uterine fibroids may increase in size. In metabolic or endocrine disorders, careful clinical preevaluation is indicated. A few patients without evidence of hyperthyroidism had elevated serum protein-bound iodine levels, which in the light of present knowledge, does not necessarily imply hyperthyroidism. Protein-bound iodine increased following estrogen administration. Bromsulphalein retention has occurred in up to 25% of patients without evidence of hepatic dysfunction. Studies from 24-hour urine collections have shown an increase in aldosterone and 17-

ketosteroids and decrease in 17-hydroxycorticoid levels. Thus, Norinyl should be discontinued prior to and during thyroid, liver or adrenal function tests. Because progestational agents may cause fluid retention, conditions such as epilepsy, migraine and asthma require careful observation. Thus far no deleterious effect on pituitary, ovarian or adrenal function has been noted; however, long-range possible effect on these and other organs must await more prolonged observation. Norinyl should be used with caution in patients with bone, renal or any disease involving calcium or phosphorus metabolism. **Side Effects:** Intermenstrual bleeding; amenorrhea; symptoms resembling early pregnancy, such as nausea, breast engorgement or enlargement, chloasma and minor degree of fluid retention (if these should occur and patient has not strictly adhered to medication plan, she should be tested for pregnancy); weight gain; subjective complaints such as headache, dizziness, nervousness, irritability; in a few patients libido was increased. In a total of 3,090 patients, 2.2% discontinued medication because of nausea.

**NOTE:** See sections on contraindications and precautions for possible side effects on other organ systems.

**Dosage and Administration:** One Norinyl tablet orally for 20 days, commencing on day 5 through and including day 24 of the menstrual cycle. (Day 1 is the first day of menstrual bleeding.)

**Availability:** Dispensers of 20 and 60 tablets; bottles of 100.

**References:** 1. Council on Drugs. JAMA 187:664 (Feb. 29) 1964. 2. Brvans, F. E.: Canad Med Ass J 92:287 (Feb. 6) 1965. 3. Goldzieher, J. W.: Med Clin N Amer 48:529 (Mar.) 1964. 4. Cohen, M. R.: Paper presented at Symposium on Low-Dosage Oral Contraception, Palo Alto, Calif., July 15, 1965. Reported in Med Sci 16:26 (Nov.) 1965. 5. Hammond, D. O.: Ibid. 6. Rice-Wray, E., Goldzieher, J. W., and Aranda-Rosell, A.: Fertil Steril 14:402 (Jul.-Aug.) 1963. 7. Goldzieher, J. W., Moses, L. E., and Ellis, L. T.: JAMA 180:359 (May 5) 1962. 8. Kempers, R. D.: GP 29:88 (Jan.) 1964. 9. Tyler, E. T.: JAMA 187:562 (Feb. 22) 1964. 10. Rudel, H. W., Martinez-Manautou, J., and Maqueo-Topete, M.: Fertil Steril 16:158 (Mar.-Apr.) 1965. 11. Flowers, C. E., Jr.: N Carolina Med J 25:139 (Apr.) 1964. 12. Goldzieher, J. W.: Appl Ther 6:503 (June) 1964. 13. The Control of Fertility. Report adopted by the Committee on Human Reproduction of the American Medical Association. JAMA 194:462 (Oct. 25) 1965. 14. Flowers, C. E., Jr.: JAMA 188:1115 (June 29) 1964. 15. Merritt, R. I.: Appl Ther 6:427 (May) 1964. 16. Newland, D. O.: Paper presented at Symposium on Low-Dosage Oral Contraception, Palo Alto, Calif., July 15, 1965. Reported in Med Sci 16:26 (Nov.) 1965.

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## LSD Warning Still Applies

Most of those who have suffered ill effects from taking the drug, LSD (lysergic acid diethylamide), probably didn't listen to the advice of physicians.

As early as September, 1963, an editorial in the *Journal of the American Medical Association* warned of possible dangers in the hallucination-producing agents, including LSD.

The advice still applies, says the author, Dana L. Farnsworth, M.D., director of health services and the H. K. Oliver Professor of hygiene at Harvard University.

"Recent clinical observations . . . suggest that people who are attracted to the hallucinogenic drugs are often those most likely to be harmed by them," said Dr. Farnsworth's 1963 editorial.

"Many who have tried the drugs were persons who had difficulty dealing with reality, who sought in drugs a quick and easy method of changing reality, and who hoped for a prompt solution to their inner conflicts."

Experience with patients demonstrated "beyond question," Dr. Farnsworth said, that the hallucinogenic drugs "have the power to damage the individual psyche, perhaps to cripple it for life."

There is no easy way to identify those for whom the drug is "safe," he said. Neither can it be foretold which person will suffer ill effects from the drugs; their effects seem to vary from time to time on an individual.

"Numbers of people promoting the hallucinogens are not aware of, and evidently do not care about, the harm caused by their use," Dr. Farnsworth said. "These persons typically pay little attention to precautions that any responsible investigator would demand."

Dr. Farnsworth listed statements of patients and witnesses that tell a great deal about the hazards of LSD:

"—I kept a journal while on the drugs. Later I read it and it was horrible. People were tearing each other apart. Also, I felt I was reading the worst pornography I had ever read."

"Your mind seems to think about all the things it ordinarily doesn't want to think."

"—I had a compulsive urge to do violence to my children . . . nor do I know how great the gap was between the violent thoughts in my mind and their possible execution."

Said Dr. Farnsworth: "Those promoting the general use of these hallucinogens believe they 'expand consciousness' and give a man or woman new in-

sights and new intellectual powers. Such testimony is common and makes it easy to understand the fascination these drugs exert on many people, especially on those of college age.

"On the claim that the hallucinogens 'free' the mind for creative work, it must be said that up to now we have had any amount of rhapsodic talk and writing, but no responsible proof. Meanwhile, the evidence accumulates steadily to indicate that the drugs do exert powerful and often damaging effect on the human system," Dr. Farnsworth said.

A new book by Dr. Farnsworth, "Psychiatry, Education, and Young Adults" is being published by C. C. Thomas Company. A chapter is devoted to LSD and other hallucinogenic drugs, in which these warnings are repeated.

The AMA's Council on Mental Health, of which Dr. Farnsworth is a member, urges all physicians to be on the alert in their communities for these drugs. The only legal source of supply of LSD, a drug manufacturing firm, recently ceased supplying medical researchers, thus, any manufacture and use of LSD is now done without legal and medical authority.

"Until adequate controls are formulated," Dr. Farnsworth said "every physician has a duty to help prevent the unwise distribution of substances which are a real menace to mental and physical health.

## Artificial Human Insemination Discussed

It probably never will be widely accepted, but artificial human insemination is a legitimate scientific procedure to fulfill a childless wife's deep need to have children, says an article in a current publication of the American Medical Association.

Artificial insemination "is being done by ethical physicians who are aware of the dangers and need for safeguards in this procedure, and it seems likely to continue this way," said Bernard Rubin, M.D., Chicago, in the current *Archives of General Psychiatry*.

"Women have a psychobiological drive . . . toward bearing children," Dr. Rubin said, "and within a barren marriage due to a husband's infertility, artificial insemination would offer the most satisfying answer to that drive."

Strong fears, however, probably will prevent the procedure from becoming an institution of society, Dr. Rubin said.



Anatomy of  
Low Back Pain #1



**the sedentary life  
is often the seat of  
low back pain**

The human spine is not engineered for prolonged sitting at desks, pianos, typewriters and drafting boards. The stresses set up by the heavy, forward-tilted head and trunk, balanced precariously on an insufficient base, result in strain of the dorsal musculature, particularly at the low lumbar level.

*The unusual muscle-relaxant and analgesic properties of 'Soma' make it especially useful in the treatment of low back sprains and strains. 'Soma' is widely prescribed ☐ to relieve pain ☐ to relax muscles ☐ to restore mobility.*

**Indications:** 'Soma' is useful for management of muscle spasm, pain, and stiffness in a variety of inflammatory, traumatic, and degenerative musculoskeletal conditions. It also may act to normalize motor activity in certain neurologic disturbances.

**Contraindications:** Allergic or idiosyncratic reactions to carisoprodol.

**Precautions:** 'Soma', like other central nervous system depressants, should be used with caution in patients with known propensity for taking excessive quantities of drugs and in patients with known sensitivity to compounds of similar chemical structure, e.g., meprobamate.

**Side Effects:** The only side effect reported with any frequency is sleepiness, usually on higher than recommended doses. An occasional patient may not tolerate carisoprodol because of an individual reaction, such as a sensation of weakness. Other rarely observed reactions have included dizziness, ataxia, tremor, agitation, irritability, headache, increase in eosinophil count, flushing of face, and gastrointestinal symptoms.

One instance each of pancytopenia and leukopenia, occurring when carisoprodol was administered with other drugs, has been reported, as has an instance of fixed drug eruption with carisoprodol and subsequent cross reaction to meprobamate. Rare allergic reactions, usually mild, have included one case each of anaphylactoid reaction with mild shock and angioneurotic edema with respiratory difficulty, both reversed with appropriate therapy. In cases of allergic or hypersensitivity reactions, carisoprodol should be discontinued and appropriate therapy initiated. Suicidal attempts may produce coma and/or mild shock and respiratory depression.

**Dosage:** Usual adult dose is one 350 mg. tablet three times daily and at bedtime.

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The strongest of these is the fear of an incestuous marriage between the child and the semen donor or his family. This is possible because the donor's identity is traditionally kept secret by the physician.

The fear seems to be stronger than any other medical, legal, or religious consideration, Dr. Rubin said. Opinions are mixed, however, on these other aspects of artificial insemination.

Jurists and lawyers question whether a child born of artificial insemination is legitimate or illegitimate. They also have mixed opinions on the legal responsibilities of a physician who performs the procedure.

Three lower courts in Illinois have considered artificial insemination. One stated it constituted adultery for purposes of divorce, and two others stated it did not. A Scottish court in 1958 ruled that artificial insemination did not constitute adultery, while an English court held that it did.

There actually are two kinds of artificial human insemination: Semen may be obtained from the husband, and its use in this way is called homologous artificial insemination (AIH). Or semen may be obtained from a third party, or donor, and its use is called heterologous artificial insemination (AID).

AID is often tried in cases of male sterility, to prevent hereditary disease transmission, or for eugenic reasons. This is the most frequently used procedure, the one in which incest is a possibility, and the one most often reacted against.

A group of 85 women, all of whom had been artificially inseminated at a midwestern university center, were contacted by questionnaire. Of the 43 who responded, "only three suggested conflict with their husbands about this," Dr. Rubin said.

"What seemed important to these couples was that 31 of 43 included their husbands in the entire procedure so they felt a part of it, and reported it added to the fathering response," he said.

The time needed to conceive by artificial insemination was 1 to 27 months (average 5.6).

Three women had children by natural insemination, following which their husbands became infertile, and they then had later children by artificial insemination. One had a natural insemination in a previous marriage. One had two children by natural insemination, and a third by AI. One mother had adopted two children and then had one by AI.

When compared to a similar group of 43 women who had had natural pregnancies, "there were almost no significant differences in (the women's) development as children, adolescents, and women," Dr. Rubin said. No psychological illness was present in either group.

The only major differences among the two groups of mothers were the fantasies they enter-

tained about whom the child resembled. Six of the artificially inseminated women strongly protested their child did not resemble any member of their family, particularly not the male members of the mother's family. Nineteen other AI mothers said their children resembled their own father, uncle, or brother. Only one naturally inseminated mother expressed this.

## Parent Loss Effects Vary

Loss of a parent sometimes results in juvenile delinquency or school dropout—but may also stimulate some children to extra achievement.

These are findings in two reports in the current Archives of General Psychiatry, published by the American Medical Association.

The author of both reports, Ian Gregory, M.D., Columbus, Ohio, found that of students referred to him for psychiatric consultation at a small midwestern liberal arts college, a higher-than-average percentage had lost a parent from death or divorce. Of these, a much higher than average percentage had parents who were divorced.

At the same college, however, two students who had lost a parent by death were among seven who were graduated with highest honors over a five-year period. The figure is admittedly small, but has some statistical significance, the author says.

"This combination of rare events is unlikely to have occurred by chance, and suggests that factors associated with bereavement may lead some students to strive for exceptional achievement," Dr. Gregory said.

He also surveyed a statewide sample of 11,329 Minnesota ninth-grade school children and found that:

Delinquency in boys was much more frequent than average among boys who had lost their father by separation or divorce.

Delinquency was somewhat more frequent than average among boys who had lost their father by death.

Delinquency in girls was more frequent among those whose parents had been separated or divorced, those who had lost their mother by death, those who were living with father only, and those who were living with neither parent.

Girls who lost their mothers and boys who lost their fathers got into more trouble than children who lost parents of the opposite sex.

High rates of high school dropouts were found among both boys and girls whose parents had been separated or divorced, and those who lost a parent of the same sex by death. Among non-delinquents, however, school dropout is more strongly related to intelligence and socioeconomic status than any other factor.



## **New Technique For Aiding Infant Breathing**

Mechanically assisting the breathing of a newborn infant has long presented difficulties.

Many babies die who might have survived if a way could have been found to keep them breathing in the first days after birth. Others survived, but suffered brain damage.

Five physicians report a technique in the current (July 19) *Journal of the American Medical Association* which in early trials has shown a high percentage of success in aiding infants with breathing difficulties.

The idea is simple: a soft plastic tube attached to a mechanical respirator is inserted through the baby's nose and into his trachea. It is kept there for several hours or days until the baby's body can fight off infection or drug imbalance and take over its own breathing.

Oxygen-enriched air with high humidity and at relatively high pressure is administered. The respirator's speed is increased for an infant's rapid breathing.

The difficult part of the procedure is the close attention which must be given the infant and the respirator throughout the long period of breathing assistance. The attention is equal to that given a surgical patient under anesthesia, the authors report.

This method of respiration has "important advantages" over inserting a breathing tube through a trachea incision, the report said.

"First, respirator treatment can be started simply and speedily. Second, it can easily be discontinued if the infant seems to improve."

Earlier attempts at assisting infant breathing were hampered by several factors. Most respirators designed for adults were not sensitive enough to respond to the faint breaths of such small patients.

To prevent the infant breathing out of phase with the respirator, it had been considered necessary to produce complete paralysis with the drug, curare. The authors eliminated the curare, and found that infants allowed their breathing to be adjusted by the respirator when the new technique was used.

Finally, the insertion of the tube through the nose, plus development of more sensitive infant respirators, eliminated the need for trachea incisions.

The authors point out that they are more conservative treatment in many cases of respiratory distress syndrome (hyaline-membrane disease), including control of body temperature, provision of high-humidity, oxygen-enriched atmosphere, and administration of intravenous glucose and sodium bicarbonate.

"Many infants respond to these measures, but some do not; they become cyanotic, lethargic, and die. It is for these babies, we believe . . . that intermittent positive pressure respiration has much to offer."

Newborn deaths due to simple drug depression should now be entirely preventable, the authors said. The infant can be given respiratory support until his body restores more normal chemical balance. Treatment in less common causes of severe respiratory trouble also should be effective, they said.

In the past three years, the five physicians report treating 26 infants. Eighteen survived, including one who weighed only 2.2 pounds at birth. Only one of the infants was reported to have suffered brain damage.

The authors of the report are D. Vernon Thomas, M.D., Grant Fletcher, M.D., Philip Sunshine, M.D., Irwin A. Schafer, M.D., and Marshall H. Klaus, M.D., all of the Stanford University Medical Center, Palo Alto, Calif.

## **Eye Lens Aging Of Radar Workers**

Faster-than-average eye lens aging has been found among those who work with high-powered radar equipment.

A report in a current *American Medical Association* publication points out, however, that it is impossible at present to relate this effect to vision impairment.

Two investigators from the New York University Medical Center examined 736 persons who worked with microwave equipment at 16 locations. They also examined 559 persons from the same areas who were not exposed to microwave radiation.

They found significantly greater numbers of minor lens defects among the radar workers. The defects were the same type associated with aging of eye lens, the authors said.

It was determined that certain types of radar work were associated with accelerated lens aging. Those who worked in radar research and development had greater numbers of minor eye defects than radar installers, operators, or maintenance men.

Further statistical studies indicated that it was microwave radiation, not x-radiation from radar-set tubes, which contributed to the lens aging. In fact, workers with the greatest exposure to x-radiation had the lowest incidence of eye defects.

Younger men who had worked with higher-powered equipment were found to have greater number of eye changes than some older men who had worked longer periods with lower-powered equipment.

The investigators stress that more research is needed to determine the significance of microwave radiation to lens damage.

"Occupational exposure to microwave radiation may be implicated as a stress which increases the rate of lens aging, although it is impossible at present to relate this effect to functional impairment such as loss of visual acuity or cataracts," the authors said.

### Ulcer Treatment Has Limited Value

Gastric freezing failed as a treatment for duodenal ulcers in more than nine of every ten cases studied, four Minnesota physicians report in the current *Journal of the American Medical Association*.

An 18-month follow-up of 173 cases indicates that gastric freezing has limited value in treatment of chronic duodenal ulcer, the doctors said.

In 92.5 per cent of these cases, patients had a return of symptoms or underwent corrective surgery within 18 months after their first gastric freeze procedure. Forty-two of these patients underwent a second freeze, but all had a return of symptoms.

Although freezing often fails to cure the ulcer, it does have remarkable effects on patients: it improves their emotional state.

"We have been impressed with the intense desire of many of our patients to be improved by this form of therapy, which is more vigorous than any they have previously experienced," the authors said.

It appears that "a dramatic therapeutic episode," such as gastric freezing, can improve emotional state without actually improving the physiological aspects of the disease, the physician said. In some cases, painful symptoms disappeared, even though ulcer-causing secretions of hydrochloric acid remained high.

This loss of pain response, however, could be a "prelude to catastrophe," such as a perforation of stomach wall or intestine, the authors said.

Freezing actually does reduce the secretion of acid and pepsin in the stomach, but within six to eight weeks these secretions are as high or higher than pre-freeze levels.

Thus, the authors conclude that carefully performed gastric freezing is a safe procedure for temporarily reducing acid and pepsin secretions for up to eight weeks. When compared to more conservative medical treatment, however, gastric freezing has no better record than earlier ulcer-treatment methods, the authors said.

The authors are Claude R. Hitchcock, M.D., Ph.D., Ernest Ruiz, M.D., R. Duncan Sutherland, M.D., and James E. Bitter, M.D., of the University of Minnesota Medical School and Hennepin County General Hospital, Minneapolis.

### Incident On A Nuclear Submarine

What does the ship's doctor do when the crew of a nuclear submarine is hit by severe respiratory illness?

In one instance, he did what many family physicians would: he ordered his patients to bed, told them to drink plenty of liquids, and administered cough and pain remedies. Most of the men recovered within a few days.

It was an unusual situation, however, which threatened the operating efficiency of the submarine, reported in the *Journal of the American Medical Association*. In some respects, it was an unusual infection, too.

The U.S.S. *Sam Houston*, a ballistic-missile submarine, was 26 days out on an undersea patrol when the illness began to strike. Because of operational restrictions, the submarine couldn't surface or raise its snorkel for outside air.

The close quarters of the submarine provided an interesting laboratory to study the transmission of the infection, report Lt. Robert Sawyer, M.C., U.S.N., and Robert G. Sommerville, M.D., M.C. Dr. Sawyer was the ship's physician. Dr. Sommerville is on the staff of Belvidere Hospital, Glasgow, Scotland.

Unusual aspects of the incident were that the first case of illness did not develop until 26 days after the submarine began its patrol. The second case developed nine days later. Then the infection spread rapidly, eventually affecting 16 crewmen.

They suffered headache, fever, muscular aches, and a dry cough.

After ten cases had developed, all nonessential work aboard the submarine was suspended. The outbreak was regarded with "considerable interest and trepidation," the authors said, for it was feared that the submarine's operational readiness would be impaired.

The infectious agent isolated in several of the men was *Mycoplasma pneumoniae*, which is sometimes associated with acute respiratory infections.

*M. pneumoniae* was known to have been present among the population of western Scotland when the crew arrived there to begin its patrol at Holy Loch, the report said. The curious aspect of the infection was that it waited so long—26 days—to develop.

As suddenly as they began, the infections began to level off. The ship returned to normal operation three or four days after the last crewman became ill. It was surprising, the authors said, that more cases did not develop.

The ship continued its eight-week patrol, and all of the sick crew-members had recovered by the time they were taken off on a submarine tender.





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**Precautions:** As with all new drugs, blood and liver function tests are advisable during prolonged treatment. **Pending further experience, like most chemotherapeutic agents, this drug should not be given in the first trimester of pregnancy. It must be used cautiously in patients with liver disease or severe impairment of kidney function.** Because photosensitivity reactions have occurred in a small number of cases, patients should be cautioned to avoid unnecessary exposure to direct sunlight while receiving NegGram, and if a reaction occurs, therapy should be discontinued. The dosage recommended for adults and children should not arbitrarily be doubled unless under the careful supervision of a physician. Bacterial resistance may develop.

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Connecticut State  
Medical Journal

Vol. 30 / September, 1966 / Number 9

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# Connecticut Medicine

## editorials

### Psychiatry, Medicine And The Community

Over the past 100 years the medical specialty of psychiatry has passed through many phases and, in most of these, has been more or less out of touch with medicine and the community. Indeed, the very influential Mental Health movement, with its emphasis on the broad issue of psychological well-being and dysfunction in all persons, was begun by a former mental patient and has been rather zealously para-psychiatric in its growth. However, recent developments in public attitudes and psychiatric activity have begun to close the gap between the psychiatrist and the major problems of everyday life seen by practicing physicians many times a day.

In Connecticut, there has been a tremendous community effort by thousands of citizens over the past three years in producing A Plan For Comprehensive Mental Health Services for the Communities in Connecticut. This Plan recommends multidisciplinary treatment approaches and facilities in all areas of the state, with special attention being given to children, alcoholics, the aged and public education in mental health. The long-range effects of the Plan remain to be seen, but its ambitious goals clearly spell out the need and possibility of close collaboration between psychiatry and the community at large. The Connecticut Mental Health Center described in this issue is the first large scale implementation of the Comprehensive Mental Health Services Plan.

Psychiatry's relationship with medicine is as complex as that with the community. Gregory Zilboorg, in his monumental work, "A History of Medical Psychology," published in 1941, stated:

"Psychiatry still lags behind medicine as to the certainty of its task, the sphere of its activity and the methods to be pursued. General medicine, in

the narrow sense of the word, never had to ask itself what disease is. It always knew what it meant to be ill, for both the patient and the doctor knew what pain and what other forms of physical suffering were. Psychiatry never had such a clear criterion of illness. Only a very small proportion of the mentally ill show any suffering: very few if any are aware that their suffering is caused by a mental illness."

Now, twenty-five years later, medicine and psychiatry have made some considerable progress in overcoming what Zilboorg called the "strong and deep-seated antagonism between medicine and psychiatry." He goes on to explain this antagonism:

"The language of a physical disease is universally appealing; pain, fever, a bleeding wound are understood by all. It is never difficult for the doctor to put himself in the patient's place, since he can remember his own pains and fever and cuts. He can identify himself with the patient, feel with and for him, and therefore understand him. In order to identify one's self with a mentally sick patient a totally different set of psychological reactions is required of the doctor. Every mental patient presents some form of unwillingness or inability to accept life as it is . . . Mental illness requires a singularly humanistic tolerance on the part of the doctor without which a proper identification with the patient is impossible."

Zilboorg conceptualizes the process of the physician's attempts to join forces with psychiatry as "the medical man's struggle to rise above the prejudices of all ages in order to identify himself with the psychological realities of his patients. Every time such an identification was achieved the medical man became a psychiatrist." It is my hope that the articles in this issue will illustrate the other, equally important, task of psychiatry to become more a part of medicine and the community. To paraphrase Zilboorg: it is the psychiatrist's

#### THE COVER

The recently completed Connecticut Mental Health Center at 34 Park Street in New Haven adds another dimension to the Yale-New Haven medical complex. (See Page 656.)

struggle to rise above apparent impossibility and to identify with the pathophysiological, interpersonal, sociological, cultural, legal and financial realities of his patients. Every time such an identification is achieved the psychiatrist becomes a physician and a citizen.

F. PATRICK MCKEGNEY, M.D., *Guest Editor.*

## The Somatic Mask Of Depression

Nearly 25,000 persons a year commit suicide. In reality, because of social, economic, insurance, and other legal expediences a great many more who actually commit suicide are not reported as such, but as victims of other diseases. Suicide is not due to a sudden irrational urge on the part of an emotionally disturbed person. The evidence is now conclusive that such persons do turn to their physicians and less often to the clergyman or psychiatrist for help. This means such patients seek and are able to accept psychological support. It also means that the physician needs to be alerted to any significant diagnostic clues so that he may not inadvertently overlook a case that may terminate in suicide whom he might have helped to avert this catastrophe.

Ross<sup>1,2</sup> points out that two of every three successful suicides are by patients who have suffered from depression or chronic alcoholism. Thus there is little question that depression is the single most reliable clue to a potential suicide and the more pronounced the symptoms, the graver the danger. Contrary to popular misconception, people who commit suicide do talk about it and one should pay careful attention to such statements as "I would be better off dead" or life is "not worth living." Depression in fact is so frequent a precursor to suicide that physicians need to be acquainted with forms of depression most frequently encountered.

There are various deceptions in the recognition of depression: A patient who has numerous complaints but no discernible organic basis for them. We all recognize the classical mood changes of depression characterized by despondency, hopelessness, apathy, mental and motor retardation. The patient's world outlook, life habits and bodily functions are different. This is the earliest phase of depression, an all pervasive feeling that something is wrong. Apprehensiveness or a general state of alarm are often linked to a fear of a dread disease such as cancer. There are vague non-specific physical complaints, regional aches and pains. Such a patient may rush along in his story brooking no interruption. He exhibits heightened introspection, egocentric preoccupation with minutiae. His interest is concentrated upon himself. There is an underlying downheartedness and discouragement.

We must recall here that various psychogenic states are generalized disorders affecting the patient as a whole and as such also have systemic manifestations as well as disorders of mood and emotion. In short, somatic symptoms are an important counterpart of mood changes in depression and we must learn how to lift the somatic mask of depression.

The patient usually describes a decrease or even loss of the feeling of well-being. He is tired, feels heavy, is unable to fulfill obligations of daily living. Normally the sense of fatigue that follows muscular exertion and exercise has a pleasant quality. Depressive fatigue is unpleasant, not relieved by relaxation, persistent even in the absence of exertion.

For a depressed patient sleep no longer retains its restful quality and now has become uncomfortably altered. There is early morning awakening. This goes hand in hand with depression. It is hard to get up in the morning and to dress. Though falling asleep is not the main difficulty, he sleeps lightly and is aroused easily by anxiety arousing dreams, so that he may even fear to go to sleep. When we prescribe for this insomnia we should remember that a depressed patient may use the medication for self-destruction.

It is now recognized that to many people food equals love. If a patient hates himself, he may stop eating through loss of appetite. However, it is also a fact that some mask their depression by over-eating, over-drinking or both. Whether food intake is increased or decreased the important thing is that there is no pleasure in eating. Food seems to have lost its taste, and appetite like life itself, its zest. If depression is tranquilized by food excesses then dieting may serve to expose the underlying depression and a physician should be attuned to whatever underlying states are masked by food and drink. There is no doubt that the gastrointestinal system is a notorious locus for somatic expression of a depressed state, since it exhibits almost every kind of a complaint known in organic disease of this system.

Some patients in subtle ways exhibit a need for self-punishment. Ross points out the patient who induces dentists to extract teeth and then complains that the prosthesis doesn't fit. The patient has "partially destroyed himself." He also drives to commit "social suicide" by inexorably drinking himself to ruin and death. Such behavior should be properly perceived as depressive and even suicidal in nature. In short, we need to be alert to many self-destructive aspects of a patient's life including middle-aged sexual promiscuity and escapades as





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### Warning

If coumarin-type anticoagulants are given simultaneously, the physician should watch for excessive increase in prothrombin time.

Pyrazole compounds may potentiate the pharmacologic action of sulfonylurea, sulfonamide-type agents and insulin. Patients receiving such concomitant therapy should be carefully observed for this effect.

Use with caution in the first trimester of pregnancy.

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Before prescribing, the physician should obtain a detailed history and perform a complete physical and laboratory examination, including a blood count. The patient should be kept under close supervision and should be warned to report immediately fever, sore throat, or mouth lesions (symptoms of blood dyscrasia); sudden weight gain (water retention); skin reactions; black or tarry stools. Regular blood counts should be made to guard against blood dyscrasias.

### Adverse Reactions

The most common adverse reactions are nausea, edema and drug rash. Moderately lowered red cell count may sometimes occur due to hemodilution. The drug has been associated with peptic ulcer and may reactivate a latent peptic ulcer. Infrequently, agranulocytosis, exfoliative dermatitis, Stevens-Johnson syndrome or a generalized allergic reaction may occur and require withdrawal of medication. Stomatitis, salivary gland enlargement, vertigo or languor may occur. Leukemia and leukemoid reactions have been reported but cannot definitely be

attributed to the drug. Thrombocytopenic purpura and aplastic anemia are also possible side effects.

Confusional states, hyperglycemia, agitation, headache, blurred vision, optic neuritis and transient hearing loss have been reported, as have hepatitis, jaundice and several cases of anuria and hematuria. With long-term use, reversible thyroid hyperplasia may occur infrequently.

### Dosage

The initial daily dosage in adults is 300-600 mg. daily in divided doses. In most instances, 400 mg. daily is sufficient. When improvement occurs, dosage should be decreased to the minimum effective level; this should not exceed 400 mg. daily, and is often achieved with only 100-200 mg. daily.

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well as suicidal behavior in relation to business activity.

One of the great periods of danger in a depressed patient is when he is improving. It is a time to remain vigilant and avoid lessening the patient's restrictions because this is precisely the time, as the patient's energy rises and his depression begins to lift, for him to express an underlying suicidal intent into action. During the depths of his despair and apathy, he had not the energy to destroy himself. Ross points out that extensive evidence now at hand indicates that most successful suicides occur within the three month period subsequent to the onset of improvement.

Any physician alerted to the characteristic moods indicating depression and the somatic symptoms that mask it can contribute importantly to reduce the awful loss of life that eventuates from unrecognized and untreated depression.

L.H.N.

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## The Medical Treatment Of Sexual Problems

Traditionally, one of a physician's duties to his patients is to act as a personal advisor and counselor. Few physicians would challenge that statement, yet many avoid assuming that role in their actual practice. Most physicians seem to have particular difficulty in discussing and advising their patients in matters of sexual practices or marital adjustment. There are usually several reasons for such difficulty. Most patients are hesitant to reveal conflicts or sensed inadequacies in the sexual sphere because of its heavy emotional, social and moral loading. The physician, sensing or anticipating his patient's reluctance, will frequently not inquire very specifically or thoroughly into the sexual history, just as he may "defer" a pelvic or rectal examination. In addition, the physician may hesitate in such an inquiry because he feels he is incapable of assessing the significance of whatever data he might obtain in the sexual history. If the patient spontaneously presents a chief complaint of sexual difficulty, the physician may still be at a loss since the diagnosis and treatment of sexual problems have probably not been included in his formal medical training.<sup>1</sup> In medical school he will have learned the anatomy of the genitalia and some endocrinology of the reproductive systems. However, a description or discussion of sexual inter-

course, orgasm and the varieties of sexual feelings and practice are rarely dealt with in the medical school curriculum except perhaps briefly in psychiatric courses. Even if presented in this context, little or no attempt is made to make such matters relevant to general medical practice. With this background the physician who has the interest and courage to attend to his patient's sexual problems usually must rely upon his own personal experiences with sex. These may or may not have been satisfactory to him, but they are certain to have been idiosyncratic and too limited in scope to provide a body of knowledge applicable to the wide range of patients and variety of problems in his practice.<sup>2</sup>

At this point, in view of these difficulties facing the physician, one might question the usefulness of considering a patient's sexual behavior or adjustment at all. Might it not be preferable to merely refer those patients with explicit sexual problems to specialists in urology, gynecology or psychiatry? Aside from his losing that not inconsiderable number of patients who would be so referred, the physician who does not consider his patients' sexual problems would fail to recognize factors known to contribute to many common "medical" syndromes as the "pain-prone patient,"<sup>3</sup> alcoholism and the "change of life." A full treatment of the ways in which sexual conflicts, conscious and unconscious, may precipitate or perpetuate physical complaints is beyond editorial scope. Rather, it is suggested that the practicing physician should and can develop the ability to deal with most of the manifest sexual or marital complaints presented by his patients and to obtain routinely a complete sexual history.

To aid the physician in this task, there is, unfortunately, a remarkable paucity of scientific knowledge about "normal" and "abnormal" sexual adjustment.<sup>4</sup> However, the large number of patients seen by a physician during the years of his training and practice can provide him with enough data about human sexual practices and adjustments to establish a reliable standard of comparison for evaluating an individual patient's behavior. In addition, a patient's own standards of normal and satisfactory behavior can be another important criterion of sexual adjustment. Finally, the physician must remember that not one, but two persons are involved in any sexual relationship. What satisfies the goose may not please the gander; the evaluation of marital sexual adjustment must include the feelings and expectations of both partners. As Martin concludes, "The danger to be avoided by physicians is the tyranny of the norm."<sup>4</sup>

Major complaints of sexual dissatisfaction are fairly common in medical patients, if they are given

the opportunity to present them. The physician investigating such complaints should take into account that a physical factor is present in perhaps five to ten percent of patients. The vast majority of symptoms of sexual incompatibility are reflections or manifestations of emotional disturbances in the relationship, frequently related only indirectly, if at all, to sexual intercourse. For example, conscious hostility on the part of either husband or wife toward the other is a common factor in mutual sexual dissatisfaction. In such cases, detailed inquiry into all facets of the marriage and family life often with husband and wife together, is the approach of choice.

In some cases, especially younger couples, ignorance or anxiety about sexual adequacy are major factors in dissatisfaction. A careful history from both partners, which includes the details of the sexual behavior as well as the anticipatory feelings and fantasies of both partners, can frequently identify some of these more superficial and less serious obstacles to mutually satisfactory sexual relationships. In this regard, it is important to recall that orgasm is a relative phenomenon in a psychological sense and, in the woman particularly, a very variable physiologic reaction. The best definition of orgasm might be in terms of the individual's sense of fulfillment in the post-coital phase, which will normally vary from time to time. Orgasm, may, over a long period, seem to be deficient, compared to previous experiences or as compared with a never-achieved ideal, particularly in the aging patient. In many such instances, advice regarding technique or reassurance as to the normalcy of variation in satisfaction may suffice to interrupt the vicious circle of dissatisfaction—anxiety—preoccupation—increased dissatisfaction.

Discussing a case with a psychiatrist can often assist the physician as to indications for further inquiry, advice, reassurance, environmental manipulation or recommendation of further specialized treatment. Psychotherapy or marital counseling may be indicated in more complex cases, but is frequently neither necessary nor desirable.

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## Science And The Doctor At The Bedside

It is now fashionable to raise a hue and cry over the depersonalization of medicine and medical care. Less common, but equally justified, criticism is being leveled at the increasing reliance upon diagnostic laboratory testing, to the exclusion of other, clinical methods. Yet little of this criticism is accompanied by constructive suggestions as to how to reverse this trend toward replacing the physician with symptom checklists, complete chemical, hematologic and radiologic work-ups, automatic monitoring of physical status, and even computerized history taking and diagnosis.

In a series of four papers entitled, "Scientific Methodology in Clinical Medicine,"<sup>1-4</sup> Dr. Alvan Feinstein presents cogent arguments and suggestions for a return to the scientific study of sick persons in order to define diseases, to evaluate treatment techniques, and to redirect attention to the patient's personality and his human needs.

The first paper, "Introduction, Principles and Concepts,"<sup>1</sup> traces the gradual historical shift of clinical investigation from the bedside to the laboratory, from the use of intact patients to animals or inanimate systems, in an attempt to gain greater precision and control of variables. This trend has not, however, been without its disadvantages. Much perspective and accuracy about human disease has been sacrificed by the neglect of clinical material. For example, the actual effects and efficacy of many traditional treatment methods, such as irradiation therapy or radical surgery for cancer, insulin and antibiotics, have not been clearly demonstrated despite their many years of use. Further, the current diagnostic classification system, based mainly on the observations and nomenclature of pathology, is inadequate and inappropriate to much of modern clinical medicine, both in research and practice.<sup>1</sup>

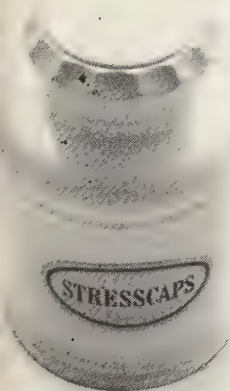
With regard to research, there are methodologic differences imposed by the laboratory and clinical situations. However, the scientific processes in both are analogous, involving experimental material, measurement techniques and appraisal of results. The clinician who makes the effort can become a "unique and powerful piece of scientific equipment." He can use mathematically sound reasoning to analyze signs and symptoms which he has carefully observed or obtained from patients and has recorded in a precise and standardized fashion. "For the scientific improvement of prognosis and therapy, therefore, research must concentrate on the old, irreplaceable clinical material—sick people—and on the old, irreplaceable equipment for observing sick people—the clinician."<sup>4</sup>





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More than twenty-five years have passed since the discovery of the diuretic activity of sulfanilamide started pharmacologists on a succession of molecular remodeling to find the ideal diuretic.

## Diuresis—a sought-after clinical effect from an unwanted side effect

It started in 1937 when a clinician reported that the administration of a sulfonamide was sometimes accompanied by an unexplainable side effect—metabolic acidosis.<sup>1</sup> Three years later the side effect was explained. The sulfonamide radical of sulfanilamide inhibited carbonic anhydrase,<sup>2</sup> the enzyme responsible for converting carbon dioxide and water to hydrogen ions and bicarbonate ions.

Later, other investigators showed by dog experiments that metabolic acidosis probably resulted when the inhibition of carbonic anhydrase upset the exchange of hydrogen and sodium ions, causing increased excretion of sodium as the bicarbonate.<sup>3</sup>

It was twelve long years after the first report of the unexplainable side effect (metabolic acidosis) that it was finally shown that large doses of sulfanilamide administered to edematous patients were indeed capable of promoting diuresis.<sup>4</sup> However, the possibility of toxic effects from its prolonged use and its relatively weak diuretic action made it impractical for clinical use as a diuretic.<sup>5</sup>

Because the inhibition of carbonic anhydrase seemed to be the key to effective diuresis, investigators began to look for more potent enzyme inhibitors—in the hopes that they would be more effective diuretics.

The most important of these early compounds, acetazolamide, enjoyed several years of fairly wide clinical use.

Its carbonic anhydrase inhibitory activity was several hundred times greater than that of sulfanilamide.<sup>6</sup> The increase in inhibitory activity, however, increased not only the excretion of sodium and bicarbonate ions, but also the excretion of potassium.<sup>7</sup> And, like its predecessor, acetazolamide precipitated mild acidosis. Its prolonged use could result in hypokalemic acidosis.<sup>7</sup>

## The 'thiazides'—an answer to the metabolic acidosis caused by carbonic anhydrase inhibition

Despite the fact that the sulfonamide

group appeared to be responsible for carbonic anhydrase inhibition which in turn appeared to be responsible for diuresis, investigators began to synthesize compounds with structural alterations to the sulfonamide group.

The first major breakthrough came with the synthesis of chlorothiazide. Altering the sulfonamide group did indeed alter the ability of chlorothiazide to inhibit carbonic anhydrase—it was only 1/10th as potent as acetazolamide in inhibiting the enzyme.<sup>8</sup> Despite the drop in inhibitory potency, however, chlorothiazide proved to be an effective diuretic—an observation that led to the conclusion that its diuretic action was due to some mechanism other than its action on carbonic anhydrase.<sup>9,10</sup>

For effective diuresis, chlorothiazide was administered in daily dosages ranging from 250 to 2000 mg.<sup>11</sup> It increased the excretion of sodium and chloride; and, to a lesser extent, potassium and bicarbonate.<sup>11</sup> The excretion of potassium appeared to be maximal at higher dose levels at which, theoretically, the carbonic anhydrase inhibitory effect is more active.<sup>11</sup> Its prolonged use, therefore, could sometimes result in metabolic hypokalemic, hypochloremic alkalosis.<sup>7</sup>

## Naturetin—effective diuresis with more favorable electrolyte balance

Other thiazides followed—with improvements being aimed at two particular areas: 1. attempts to increase diuretic action in relation to the milligram potency of the drug, and 2. attempts at a more favorable sodium/potassium ratio in the urine, i.e., to decrease the excretion of potassium while maintaining the excretion of sodium.<sup>12</sup>

One of these, Naturetin, Squibb Bendroflumethiazide, has made advances on both these points. "By adding a 3-benzyl radical to hydroflumethiazide a rather dramatic reduction in dose range is accomplished. With this drug, effective sodium excretion is obtained with

doses between 2.5 and 10 mg., which is a 200 to 1 ratio as compared to chlorothiazide..."<sup>13</sup>

Moreover, due probably to its virtual lack of carbonic anhydrase inhibition, Naturetin (bendroflumethiazide) has been shown to cause less potassium and bicarbonate loss and less alteration in urinary pH than either chlorothiazide or hydrochlorothiazide.

Naturetin is outstandingly effective not only in establishing, but also in maintaining, excretion of retained fluid in edematous patients. And its duration of action is sufficiently prolonged to allow a single daily administration in most patients. Naturetin is also an effective antihypertensive agent.

**Contraindications:** Severe renal impairment; previous hypersensitivity.

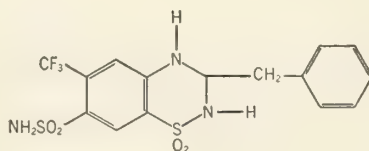
**Warning:** Ulcerative small bowel lesions have occurred with potassium-containing thiazide preparations or with enteric-coated potassium salts supplementally. Stop medication if abdominal pain, distension, nausea, vomiting, or G.I. bleeding occur.

**Precautions:** The dosage of ganglionic blocking agents, veratrum, or hydralazine when used concomitantly must be reduced by at least 50% to avoid orthostatic hypotension. Electrolyte disturbances are possible in cirrhotic or digitalized patients.

**Side Effects:** Bendroflumethiazide may cause increases in serum uric acid, unmask diabetes, increase glycemia and glycosuria in diabetic patients and may cause hypochloremic alkalosis, hypokalemia; cramps, pruritus, paresthesias, and rashes may occur.

**Supplied:** Naturetin (Squibb Bendroflumethiazide) 5 mg. and 2.5 mg. tablets. Also available Naturetin  $\bar{c}$  K [Squibb Bendroflumethiazide (5 or 2.5 mg.) with Potassium Chloride (500 mg.)]. For full information, see Product Brief.

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In his fourth paper, Dr. Feinstein eloquently emphasizes the need of the clinician to improve himself and not to allow his scientific attention to be diverted by the unbalanced use of data from the laboratory. He goes on to describe many practical and specific suggestions about achieving greater objectivity, precision, consistency, uniformity and reliability in history taking and physical examination. While these techniques of improved observation and acquisition of clinical data obviously should be incorporated into medical school curricula, they can be applied by any physician at any stage of his medical career. Indeed, it is probably the experienced, albeit tired, physician who could probably benefit most from an honest reappraisal of his own clinical practises in the light of the principles advocated by Dr. Feinstein.

An even more important reason for advocating the return to the clinical situation as being of primary value, is the need to reverse the trend of modern clinical care, which is often "focussed more on the patient's identification as a diseased organism than on his identity as a sick person."<sup>1</sup> Scientific and medical completeness demands that laboratory data about the disease be accompanied by "personal data about the patient and by clinical data about the diseased patient." The life setting, family situation and interpersonal adjustment patterns of the patient are most significant factors, influencing not only the physician's understanding of his patient, but the effectiveness of the treatment he prescribes, as well.

In this emphasis on clinical methodology, the physician must not ignore the possible sources of error due to patient unreliability of reporting or inconsistency of awareness. The patient will have the usual human difficulties in verbalizing or assigning words to perceptions which were either not assigned words when they were first noticed, or which are not easily conceptualized. Further, the patient's awareness or communicativeness may be impaired, due to organic factors connected with or separate from, any physical disease present. Finally, the patient's clear recognition and statements of perceptions of illness may be distorted by his personality, past experience and emotional state. Such variability is for instance seen in the particularly common clinical complaint of pain. Many words may be used to describe pain and each may represent a variety of perceptions, depending upon the patient's past experience, education or social class, all of which may differ from those of the doctor. These descriptions may be associated with an accompanied by a complexity of feelings having to do with the implications of the physiologic changes which contribute to the perceptions described as "pain."<sup>5</sup> Indeed, although Dr. Feinstein specifically states that these methods and principles are in-

applicable to psychiatric disturbances, his approach seems quite as appropriate to the elucidation of personality factors in illness as it is to the many other human disorders which "have no exact counterparts in morbid anatomy . . . such as abnormalities in gastrointestinal mobility and cardiac rhythm."<sup>1</sup>

These papers present concepts important to all physicians; to be disputed or corroborated; to be used as standards for self assessment of competence. Dr. Feinstein's sophisticated, lucid, enthusiastic and literate presentation is a clear and compelling statement demonstrating the imperative wedding of the scientific artistic and humanistic heritage of medicine.

F. P. McKEGNEY, M.D.

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Hysteria Through The Ages

Beginning with the concept of the wandering womb, this pathological phenomenon as well as the word itself have meandered through the medical literature and through the consulting chambers of different medical specialists with an occasional side trip into theological councils. Indeed, hysteria remains an elusive witch as crafty as any that ever burnt on the stake or stalked the envious of Salem. Besides, hysteria, or its sufferers, have seduced many a respectable physician into non-scientific pursuits, if not non-professional behavior and still perplexes and frustrates many, especially those who are uneducated about the mechanisms of conversion and of unconscious seduction, often a characteristic and prominent psychological mechanism in hysterics.

While it is often claimed that hysteria is a vanishing entity, and this is corroborated by survey of psychiatrists in private practice in recent times,<sup>1,2</sup> this is like a school dentist in a community with fluoridated water claiming that dental caries is on the decline generally. Major hysterical symptoms certainly have disappeared from psychiatrists' offices and are rare in Western middle and upper socio-economic groups. No doubt perfusion of

Breuer's and Freud's discoveries into general knowledge absorbed now by most every high school student has greatly contributed to the blocking of florid and dramatic hysterical behavior. However, the mechanisms, the basic psychopathological processes characteristic of hysteria still are seen or heard often by the psychotherapist, and just like "classical lobar pneumonia" can still be encountered, so can classic or major hysteria. The psychiatrist, however, is not likely to see it unless he goes to the emergency rooms of our large municipal hospitals or visits on other non-psychiatric services in the general hospital, especially the neurological divisions. In the Eastern United States he might have to concentrate particularly on the non-white population, but in lower class patients all of "classical hysteria" can still be seen, the convulsions, the contractures after misdiagnosed hysterical paralysis, double vision in one eye, hysterical blindness, aphasia and abasia astasia.

The reason for pointing this out in some detail is to point out a common confusion. In our eagerness to emphasize the medical nature of mental illness as distinct from criminal or sinful behavior, this assertion is taken to mean that hysteria (or psychosis or alcoholism) is like any other disease. Because hysterical people should be treated like patients, as people in need of help and treatment, does not mean that hysteria is the same as pneumonia or diabetes. Hysteria is a defective development of the personality, and the toxic agent or agents are psychosocial vicissitudes with or without some physio-chemical readiness of the central nervous system to react—or perform—"hysterically," i.e. to convert emotional conflict into bodily dysfunction of an inhibitory type. Cultural factors may also play an important role and the condition can be "contagious." The development of hysterical defenses or character structure, therefore, is always one possibility of many types of personality development and therefore will not disappear from the ecological structure of personalities.

This relatively simple deviation of psychic processes can be produced experimentally by any hypnotist, but this should not deceive one to assume that the condition, and the treatment of hysterical patients is simple. It must be noted, however, that this treatment is often iatrogenically jeopardized by the frequent insistence of searching for every remotely conceivable organic cause to account for hysterical symptoms. This subjects the hysterical patient to many tests, each an inadvertent accentuation of his resistance to consider his symptoms as conflict-engendered behavior. A positive diagnosis of hysteria can usually be made through an adequate history and appropriate evaluation of the

socio-emotional climate in which the symptoms appeared—sometimes strongly suggested by the presence of similar symptoms in a person significantly related to the hysterical patient. But the physician must understand that disease is something that occurs, not only in the form of infections or metabolic defects, but also as faulty personality development and structure, and that understanding and treating these aspects of humans is as much a medical task as dispensing antibiotics or removing tumor cells. Major hysteria will not disappear unless all people become educated and psychologically sophisticated, a task in which physicians can and must participate as professionals and as citizens, but hysterical mechanisms in more subdued forms will probably remain with us until we can prevent effectively the development of neurosis, a very unlikely eventuality in the foreseeable future.

STEPHEN FLECK, M.D.

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## Ontogenesis Of REM Sleep

Reptiles and tortoises do not show REM sleep. Birds seem to have brief periods but the mechanism is highly developed in mammals and is located in the caudate nucleus of the pons. Why did the pons become the site of the REM sleep mechanism and what function requirement was met by development of REM sleep phylogenetically. We have already seen that there is a physiological need for REM sleep in adult subjects who when deprived of it exhibit bizarre and even psychotic behavior. Such subjects after a time exhibit a dramatic rise in the amount and percentage of the REM phase—they show a tendency to compensate for lost REM sleep after artificial interruptions of sleep.

What came as a surprise to investigators was the discovery that REM phases of sleep are not limited to adults, but assume a high proportion of total sleep in the first days of life.<sup>1</sup> In the neonate sleep commences with a REM period and the EEG is not different from the wakeful state. Furthermore, the neonate spends fully half of its total sleep in this unique state of activation. In premature infants the percentage of REM sleep is 58 to 36-38 weeks, 67 at 33 weeks and 80 at 30 weeks, and probably nears 100 per cent before the 30th week. How can this discovery be explained, why does REM drop off progressively with age (see figure on Front Cover).





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<sup>1</sup>. Collective studies, Department of Medical Research, Winthrop Laboratories.

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It is known that the cortex sends inhibitory impulses to many subcortical areas. The brain stem in turn sends stimuli to both cerebral hemispheres, and each in turn feeds back restraining forces upon the brain stem. One explanation of the disproportionate large amounts of REM sleep in the developing fetus and neonate might be that the brain stem matures early while an immature cortex is not developed sufficiently to exercise restraint upon the pontine sleep center. However the pontine mechanism is at least partially autonomous since removing the cortex does not increase REM but may decrease it. It may of course be that as the adult matures and grows old the cortex does exercise more and more restraint upon the dream center in the pons thereby reducing the total amount and percentage of REM in total sleep.

We are still however left with the question as to what can be the organism's need for this REM state at each stage of its growth and development. One thought would be as Roffwarg, et al. believe, that in early infancy when waking life is limited in time and scope and offers little occasion for stimulation, the REM period furnishes a substantial and necessary discharge of activity, and its diminution as the organism grows older, is that its most important function in early ontogenesis has been fulfilled. Another view would be that at different stages of development it serves different functions. In late fetal life and early infancy it furnishes necessary discharge of activity into the cortex to promote its maturation and myelination. In adolescence when there is a modest increase in proportion of total sleep spent in REM periods, they could serve to permit discharges of instinctual urges without interrupting sleep and thus free the individual from irrational behavior during waking life. As instinctual drives decline in later life the need for REM periods also decline.

We have traditionally considered the sleep of babies as well as adults to constitute a surcease from excitation, a time of rest, a reversal of fatigue, an opportunity for metabolic restoration. In this conventional view the infant either sleeps and is separated from external stimulation or he is awake and receptive to it. But now we are aware that during REM sleep brain activity is vigorous. The stimuli begin in the caudate pons and travel upward through the thalamus to higher centers causing both excitatory and inhibitory effects, rapid eye movements (REM), flaccidity of peripheral muscles, respiratory and heart rate changes and probably others. Thus REM sleep affords intense stimulation to the central nervous system, stimulation turned on and off rhythmically from an autonomous mechanism in the pons. As Roffwarg, et al. state so aptly, the dream is "born in the brainstem but clothed in the cortex."

If we seek for a purpose of REM in early development, then the concept of "stimulus induced development" assumes especial significance. Romanes points out that visual pathways of sleep become myelinated before light reaches the retina. It is possible that structural maturation in the other sensory systems during fetal life as well as the visual system may depend on discharges emanating from the pontine center. Furthermore the concept of stimulus induced development might help to explain the importance of REM periods as a prime source of cortical stimulation in early ontogenesis.

Many have the idea that the immature central nervous system can anticipate or prepare for its future active role long before such functions are called into play. Can the abundance of REM stimulation in the cortex in early development account for the tremendous growth of the central nervous system in the first year or two of life. If this be true then we can understand that the REM mechanism became necessary in phylogenetic evolution at the time that extensive telencephalization began. It served to maintain large masses of neural tissue before they became involved in motor and sensory reactions taking place during sleep.

Areas in the central nervous system which are myelinated in utero are those that receive afferent fibers directly from subcortical centers. The most differentiated and mature cells are found in the brain within the primary sensory areas, principal motor areas, limbic system and rhinencephalon. All these areas are intimate participants in the neurophysiology of the REM state. The mechanism, reasons Roffwarg, et al., may then function to bring higher centers to an operational capacity sufficient for handling the rush of external stimulation in waking experience.

A physiological system that remains active throughout life as the REM system does probably continues to execute physiological as well as psychological functions. The natural physiologic function might be that frequent excitation of the higher brain centers during REM sleep serves to maintain the central nervous system in a state of physiological readiness so that it may react swiftly to the exigencies of the real world. This means that extended interruptions of excitation may be injurious to optimal responsiveness of neural structures. We have an analogy from studies on depth perception, whose accuracy is considerably weakened after one eye has been covered for a matter of hours. In this sense then the stimulating function of the REM mechanism may remain important to the organism throughout life.

From the psychological point of view, it is known that deprivation of REM sleep induces certain behavioral and psychological aberrations in humans. During REM the muscles are inhibited

while the cortex is active. REM serves then to maintain the individual in sleep as Freud emphasized. During REM instinctual drives seek and achieve symbolic gratification. Without REM perhaps instinctual urges might dominate waking life and make normal function impossible. The experiment producing hypersexuality in REM deprived cats is especially pertinent in this regard.

If Roffwarg's hypothesis on the role of REM as promoting maturation of the cortex and keeping it efficient has validity, as it probably does, then the developing fetus should show critical failures or lags in maturation of certain neural systems if deprived of the REM state. In addition, a significant reduction of external sensory input to the developing nervous system, might by means of a feedback system retard the rate of diminution of the REM moiety. Such hypotheses are now ready for experimental verification.

L.H.N.

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## Neurophysiology Of Dreams

Until the last decade, dreaming was knowable through analysis of subjective experiences. Freud's brilliantly intuitive and analytic deductions led to the concept that dreams were hallucinatory experiences in which instinctual discharges occurred in the form of symbolic fulfillment of a wish and at the same time it permitted uninterrupted sleep. Now that we have learned how to recognize the dreaming sleep through recordings, rapid eye movement REM and a special change in the electroencephalogram (EEG), the process has become accessible to objective investigation.

A normal adult 50-70 minutes after falling asleep enters the dreaming period. These recur every 80-90 minutes and comprise 25 per cent of the conventional night's sleep of young adults. The REM periods are short in the early night and longer towards morning, averaging 20 minutes in length and recurring 4-5 times. The dream state of sleep (REM) is singularly distinct from the non-dreaming sleep NREM. During non-dreaming sleep respiration, heart rate, and blood pressure is basal, but display greater variability during dreaming. Here the muscle tone from head and neck virtually disappear, but the ocular muscles are an exception because during dreaming there is rapid eye movements (REM). Penile erections are specific in the REM period and detumescence ensues in the NREM period.

The EEG during REM sleep is remarkably similar to that of a subject awake under circumstances

of visual imaging or stimulation. Similarly cortical responses evoked during the waking state are extremely similar to those evoked during REM sleep. There is a lowered responsiveness to stimulation during REM sleep at the same time there is also greater spontaneous activity in the reticular formation which perhaps is the reason that evoked responses are occluded.

Every species of mammal so far studied exhibits rhythmically alternating periods of REM and NREM activity in most respects similar to those found in man. During REM there is increase in blood flow in the cortex, rise in brain temperature, elevation in frequency of spontaneous neuronal firing in the reticular formation, descending vestibular nuclei, pyramidal tract, and in the occipital (visual) cortex. During REM sleep thalamic and cortical neurones are more responsive than they are during the waking state. As the thalamic and cortical neurons are more responsive there is an active inhibitory effect on spinal reflexes and resting muscle tone. The unique quality of REM sleep is that it is a time of considerable excitation within the brain which is largely blocked at the periphery. Probably this inhibition of motor and reflex activity allows perpetuation of behavioral sleep at a time when areas of the brain are discharging at frequencies approximately those during wakefulness. Thus we have neurophysiologic confirmation of Freud's postulate that dreaming allows for perpetuation of behavioral sleep.

The question arises as to where the cortical stimulation comes from when stimulation from the periphery is blocked, and what function does it subserve. If the nucleus pontis caudalis is ablated in a cat the REM phases and low voltage fast EEG activity disappear. Such an animal will show either wakefulness or NREM sleep. The conclusion is inescapable that the pontine mechanism is necessary for REM sleep. In man also there is an analogous dependence of REM sleep upon brain stem tissue and of NREM sleep upon the cortex.

In answer to the second question, we now know that dream events have a dimension in real time although as Freud pointed out, intermediary steps in an action are missed and even distorted. Roffwarg describes a subject whose heart, during the middle of a REM period began to race and when he awakened a few minutes later, he recalled of dreams of sexual intercourse. There have also been reported elevations in gastric hydrochloric acid in peptic ulcer patients, increases of adrenal steroids during dreaming. It is clear that there is a biological relationship between mind and body. REM is not an elusive creature of the mind but an expression through autonomic peripheral activity of



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The peripheral autonomic activity are consequences of the dream hallucinations which are more encompassing than other hallucinatory events that in delirious states result from a sensory input from the environment. In the dream the total perceptual field is hallucinated. It is predominantly visual but may at times include realistic components from most sensory symptoms as well. Every nuance of emotion, as well as perception, the full world of our experience may be reduplicated in dreams. The emotions generated may be so intense as to lead to angina pectoris in patients with coronary insufficiency.

Visual information supplying the dream appears to originate within the brain stem and feeds into the visual afferent pathways at some intermediary point along the route. The brain seems to be reacting to its percepts much as an awake brain does. If the dreaming is in any sense "awake" however, it seems attuned primarily to compelling phenomena originating and being perceived within itself. Obviously for this a substantial part of the brain must be active in this state and this is confirmed by blood flow and temperature studies mentioned above. Clearly during the dreaming state of sleep without any external sensory input, "the brain is in business for itself," freed from the restraints imposed by waking living, allowed to pursue satisfaction for its instinctual wishes that it may not pursue during waking life. To succeed it needs a flaccid body which is an important component of the REM state.

There is a physiological need for REM sleep. Subjects deprived of them by awaking exhibit after a time a dramatic rise in the amount and percentage of the REM phase. They tend to compensate for the loss. Furthermore, after a number of days of dream deprivation the subjects become irritable and may even become psychotic.<sup>1</sup> If there is experimental destruction of the pons animals exhibit hyperirritability and hallucinatory-like behavior. If small amounts of REM sleep reappear these symptoms are reversed. If they don't, then animals progress to a state of insomnia, agitation, and eventually die. If there is experimental functional deprivation in cats, they show tachycardia, faster auditory recovery cycles and hypersexuality. This last symptom supports Freud's view on the need for hallucinatory sexual experiences in dreams. Could it be that they serve to prevent excessive sexual activity during waking life.

L.H.N.

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(Roffwarg—Dept. Psychiatry, College of Physicians and Surgeons, Columbia University, N. Y.)

## Critical Periods In The Organization Of The Nervous System: Role Of The Adrenal Hormone

There is evidence that the central nervous system regulation of ACTH concentration in adult rats may be a function of environmental events occurring during critical periods in infancy. With regard to the adrenal hormone, adult animals when given various forms of stimulation during a critical period in infancy differed markedly from non-stimulated animals in the temporal pattern of their steroid response to acute noxious stimulation and the magnitude of their steroid response to novel stimulation or novel experience.

The observations themselves are clear enough. Handling an infant rat by picking it up daily, placing it in another cage for three minutes, and then returning it to its nest produces profound changes in its response to stress as compared to animals not so treated. When animals reach adulthood, the handled ones show a more rapid and greater steroid response to a brief but intense electric shock, than do the non-handled ones. The latter respond more slowly and the response persists over a much longer period of time. The handled ones in infancy when grown up explore more freely, defecate less in a novel environment than the non-handled controls do.

Levine and Mullins<sup>1</sup> performed two kinds of experiments. Handled infant animals when exposed to cold showed a significant depletion of adrenal ascorbic acid several days earlier than the non-handled animals. Similarly rats as young as three days old, if handled show a significant increase in adrenal steroids following electric shock. No such increase was found in non-handled infant rats until they were at least nine days old. These investigators also found that handled animals show a greater steroid output after ACTH injections either six or nine days after birth.

Thus they found changes in the adrenal steroid levels in the handled rat at a time during development when the central nervous system mechanism that control physiological functions in the adult are not yet permanently established.<sup>2</sup> The question which now arises concerns the nature of the physiological processes in the newborn animal whereby handling in infancy can permanently affect the adrenal system so that the adult animal can respond more appropriately.

We know that controls of adrenal cortical function in the adult organism is partially accomplished

by means of a homeostatic feedback mechanism or hormonostat. In such a system the concentration of corticosteroids in the blood is monitored in the central nervous system and compared with a controlling set point. If the concentration of circulating steroids is higher than this set point, then ACTH secretion and therefore adrenal output diminishes. If the concentration is below this set point then ACTH is released and more steroids are produced.

In this hormonostat, the set point can vary to some extent and is not fixed at a definite level. In this way the hormonostat can react to varying demands of the environment as well as the inner requirements of the organism. If there are several values to the set point, then the sensitivity of the hormonostat is enhanced and can respond anywhere between the minimum values which corresponds to the concentration of steroids when the animal is resting and in a graded manner to its maximum value which would correspond to the concentration of steroids under conditions of extreme stress.

We may then hypothesize that handling, by causing variation in the concentration of adrenal steroids in the infant animal modifies the set point during a critical time in development, so that it can vary in a graded manner in the adult with several possible values between the minimum and maximum. If this were true then it could explain why handled rats in infancy, when they are adult are able to respond to novel, but not physically threatening stimuli such as the open field with a moderate increase in adrenal steroid production and with a large and rapid increase to shock.

In the non-handled newborn rat there is less variation in steroid concentration during the critical period and the set-point develops fewer possible values. Their hormonostat tends to operate either at "resting" level if there is no change in the environment, or at levels close to maximum if there is any change at all, whether or not the change is physiologically threatening. If the mother is disturbed during the handling of the infant this can also produce variation in the concentration of steroids in the infant. Presumably the resulting variation in the mother's steroids are communicated to the young possibly through the milk. In any way we look at it handling in infancy tends to reduce emotional reactivity in the adult organism grading it in accordance with stimulus input.

In the rat the circulatory portal system between the median eminence of the hypothalamus and the pituitary is not developed before the animal is five days old so that the feedback mechanism of the type found in the adult could not be operating in the newborn animal. It would however appear from the handled animal experiments that adrenal steroids in the newborn animal play an important role in

determining the sensitivity of the brain areas which control adrenal functioning in the adult.

Implicit in the foregoing discussion is the notion that there are specific time periods in development during which particular types of stimulation will have profound and irreversible effects upon the physiology and behavior of the adult organism. A corollary of this hypothesis would be that before or after the critical period, a particular type of stimulation will have little or no effect.

But the idea is more pervasive than involving just one system. For example, handling animals between two to five days, was found by Reisner and Levine to cause no increase in the blood glucose levels on adult rats after an electric shock. In non-handled animals shock caused higher blood sugar levels than in those of the controls. Here we have an instance where the same treatment of a newborn rat has an effect on two physiological measurements in adulthood.

Levine found critical periods for other parameters also. For example a single exposure to extreme cold within the first 12 hours after birth improved avoidance conditioning in adulthood as compared to a single handling experience during the same period which was without effect on avoidance learning later. Other ideas are also developing with regard to the "critical period." Denenberg<sup>3</sup> reported that the intensity of the infantile experience may be an important determinant of the critical period. He demonstrated that rats handled from days 1-3, 3-5, and 1-5 of life did not differ from controls in avoidance learning whereas animals shocked on those days did differ from controls. Their experiments make it seem reasonable to postulate at this time that changes in the central nervous system do occur when stimulation of varying types are applied during critical periods of development.

Scott<sup>4</sup> has already shown that there are at least three aspects to the concept of critical periods. One dealing with the formation of basic social relationships; another for optimal periods of learning and a third involving infantile stimulation such as is dealt with in the findings above. The results discussed are only a beginning of what will eventually be a long list of interactions among the neuroendocrine systems at all stages of development.

The elucidation of these processes should bring us much closer to an understanding of the intimate relationships between physiology and behavior. Ultimately such knowledge will be extended to discovering the critical periods in behavioral development of our children so that we can make maximum use of their potentialities limited only by the physiology and structure imposed by heredity.

L.H.N.





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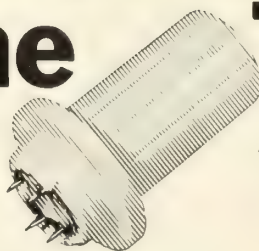


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## Critical Periods In The Organization Of The Nervous System: Role Of Gonadal Hormones

The rat is an excellent animal for studying hormonal influences on the organization of its nervous system. When they are born they are females physiologically but are capable of differentiating into males if testes are present. If males are castrated at birth and thus deprived of testosterone, the animals will grow up to show complete female receptive behavior in response to administration of estrogen and progesterone in adulthood. If, however, they are castrated after the first five days of life this will not happen. The first five days of life then seem to be a "critical period" during which gonadal hormones in the newborn rat profoundly and permanently affect the animals subsequent biological functioning.

The steroids present in the infant also determine to what hormones the brain centers controlling sex behavior in the adult will be responsive. A large dose of estrogen given in the first 120 hours to female rats seems to damage the development of the controlling brain centers, since they become incapable of responding normally to the female sex hormone in adult life. In fact such treated infants sometimes show complete male sex behavior pattern in response to testosterone in adulthood. Their sexual receptivity was abolished.

Female rats if given minute doses of androgen as little as five micrograms during the first five days of life suffer disruption of their normal female development. The gonadotrophin releasing mechanism of the central nervous system is converted from a cyclic to an acyclic one. Ovulation is blocked although such females are constantly sexually receptive. However, the degree of sexual receptivity will vary inversely with the size of the neonatal dose. Moreover even though the females remained sexually receptive, their sexual behavior was quite aberrant.

Male rats given estrogen in infancy also show marked defects in sexual behavior. Such rats show a great deal of mounting behavior, rarely achieve intromission and never ejaculate.<sup>1</sup> However, such an

experiment does not help much in invoking a change in the central nervous system organization to explain such behavior because there is a concomitant marked atrophy of the reproductive system. But as we have seen castration of the newborn male rat does markedly alter sexual behavior since it exhibits complete female sexual behavior if it receives estrogen and progesterone at low doses in adulthood. Males castrated in adulthood show no such behavior after this procedure.

The rat is not the only animal exhibiting critical periods in sexual development. Guinea pigs do also but to modify their nervous system organization, it is necessary to inject testosterone propionate into the uterus prenatally in order to effect masculinization of the female offspring. In this animal the sexual organization of the central nervous system takes place before birth. It is therefore not as convenient a test animal for study as is the rat whose critical period for the organization of the nervous system to control adult sexual behavior is in the first five days postnatally.

How can such results be explained. One suggestion is that gonadal hormones exert a dual influence on the central nervous system. The first one which is organizational occurs during the critical period of development which is the first five days in the rat. At this time the brain is sexually undifferentiated. Depending upon the hormones present the central nervous system will become organized so that an acyclic or male pattern of hormonal release will occur in the male adult, or a cyclic pattern of hormonal release will occur in the female. These patterns can be reversed and irreparably damaged experimentally by appropriate hormonal injections during the critical period.

The second influence is the one that hormones exert in the adult that can be termed excitatory or activational. If gonadal hormones are not present in the first five days of life then the basic female (cyclic) hormone-release pattern becomes established in the adult.

Both of these patterns of hormones release can be viewed as part of a "homonostat" whereby the concentration of sex-steroids being produced "feeds back" and influences the central nervous system which in turn controls the rate of steroid production or release or both. It is not just a deficit of the amounts of hormones which causes aberrant neuroendocrine function and behavior that are observed in adult animals that were given hormones during infancy. For if such adults receive hormone replacement, the experimentally produced aberrant neuroendocrine behavior and function is not altered. The pattern set is permanent.

A probable explanation could be that the experimental procedures in infancy alters the sensitivity

of the controlling brain mechanisms with regard to the type of hormone to which it will respond in later life and also the temporal sequence of hormones to which they will respond. This pattern is obviously set during the critical period and operates in the pattern from this point on. The pattern can be normal if the presence of steroids are normal during the critical period. Or there can be produced profound and permanent changes in the subsequent psychobiological processes of the organism by experimentally varying the amount and nature of the hormone during the critical period.

If this is true then hormones in the new born must be held partially responsible for the organization of some of the central nervous system control mechanism which are destined to control the activation of these hormones in the adult.

I..H.N.

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## Salmonella In Eggs And Poultry

The number of cases of salmonellosis reported in the United States has increased dramatically in the last 20 years. Much of this is due to a greater awareness of the disease, a better utilization of existing laboratory facilities, but also to intensified epidemiologic investigations. But real increases have also occurred in the incidence of salmonellosis. The question is how can this be explained? Can it be due to the changing patterns of food consumption, particularly the greater centralization and mechanization of food processing and production? We know that these changes cause more people to be exposed at any one time to possible sources of Salmonella contamination. Lundbeck, et al. in Sweden<sup>1</sup> have given us a view of a large outbreak of the disease made possible by large-scale processing and distribution.

To gain a better understanding of the disease and improve the methods of prevention it is necessary to know the source of infection and its means of spread. One approach to this problem is the survey method whereby data are compiled to reveal both the reservoirs of salmonella organisms through the sampling of various foods and the distribution of Salmonella serotypes in these reservoirs. Wilder and MacCready<sup>2</sup> have presented rather sobering data which indicate that Salmonella could be isolated from about 40 per cent of cans of frozen whole eggs and from about 50 per cent of marketed chickens examined, including birds that had come from a government inspected poultry processing plant.

Fourteen different Salmonella species were recovered from the chickens during the survey.

Studies of two processing plants, one government inspected and one not, suggest that they did not serve as a medium for the growth of a given Salmonella species but rather that new species were constantly being introduced with the incoming fresh poultry. Thus if an individual bird was not contaminated before arrival, it stood a reasonable chance of picking up the Salmonella during processing with other birds. As the *New England Journal of Medicine* points out "one might rightly wonder not so much at the increasing incidence of Salmonellosis but why everyone does not already have the disease."

In the first place many of us may have had the disease in a light form with transient diarrhea and low grade fever and promptly recovered. Then there is the well known fact that a large inoculum ( $10^6$  organisms) is necessary to establish the disease in man and this may afford some increase of protection. Certain host factors however such as gastric surgery, antibiotic therapy, infancy and debility may markedly alter this relation.

Salmonella are killed by the proper cooking of eggs, poultry, meat, and other foods, and this would properly protect an individual from contracting the Salmonella infection. However we should remember that a soft-boiled egg (four minutes in boiling water), may be tasty but the Salmonella within have not necessarily been destroyed by this type of cooking.<sup>3</sup> Then there is the potential role of raw egg as in egg nogs or under-cooked eggs as a vehicle for infection. This was underscored in a wide-spread outbreak of hospital associated infection due to Salmonella derby that occurred in the Northeastern United States four years ago.<sup>4</sup> Then the common practice of thawing frozen eggs at room temperature allows for multiplication of the Salmonella organisms present and results in a highly contaminated vehicle with obvious consequences.

A further complication of the problem of Salmonella contamination of man's mass-produced foodstuffs is the recently recognized ability of the Salmonella to develop resistance to multiple antibiotics as the organisms goes through the gastrointestinal tract. This is important because multiple antibacterial drugs are now commonly used in human and veterinary medicine. To create antibiotic resistant strains by this means clearly poses a problem of increasing magnitude and clinical importance.<sup>5</sup> In short the widespread use of antibiotics such as tetracycline and ampicillin additives in feed as well as therapeutic agents in veterinary medicine may have the undesirable side effect of



ultimately creating antibiotic resistant strains of pathogenic Salmonella.

Ramsey<sup>6</sup> observed that Salmonella typhimurium isolated before 1948 were almost uniformly sensitive to tetracycline and chloramphenicol whereas in 1960, 14-29 per cent of cultures isolated from man and fowl were resistant to tetracycline. It is this development of antibiotic resistance which accounts for a protracted hospital epidemic due to Salmonella edinburg which was resistant to a multiple drug including chloramphenicol.<sup>7</sup>

The extraordinary reservoir of Salmonella in animals (practically all domestic and many wild animal species) is clearly the major source of most human disease due to this organism in this country. As a consequence of our modern way of life food is more and more mass-produced on farms, mass-prepared in processing plants and then distributed over wide areas and with it has come the undesirable Salmonella spread. In addition the disease of medical progress (DOMP) namely creating antibiotic resistant strains has seriously complicated the management of such infections once they have occurred. What then remains to be done aside from thorough cooking of the product after its purchase.

The consumer expects that a product processed under governmental supervision should be free of disease producing organisms and every effort should be made to produce a pathogen-free product. We have seen that the government inspection of the plant is not effective in detecting the presence of the organism in the product we purchase in retail outlets. If the goal of the inspection program is to produce a product free of pathogenic organisms, then a microbiologic monitoring system would have to be introduced as a part of the program. It is only

through this means that pockets of infection in the environment and poor processing techniques can be detected and appropriate steps taken to remedy these conditions.

It was encouraging to read the announcement by the United States Department of Agriculture that as of June 1965 all liquid or frozen egg products produced by plants operating under their voluntary inspection must be pasteurized or tested and found free of Salmonella.<sup>8</sup> It is now up to state regulatory agencies to follow with similar regulations for those plants not under United States Department of Agriculture inspection. This will ensure purchasers of these products a wholesome pathogen-free product similar to the status of pasteurized milk.

L.H.N.

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8. Communicable Disease Center, Salmonella surveillance report No. 35, 15 pp., Washington, D. C. Government Printing Office, March 27, 1965, p. 6 and 7.

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**Yale-New Haven Medical Center**

**Mary S. Harkness Memorial Auditorium**

**333 Cedar Street**

**New Haven, Connecticut**

**WEDNESDAY, SEPTEMBER 28, 1966**

**GENERAL INFORMATION**

**REGISTRATION:**

Registration will begin at 9:00 A.M. The registration fee of \$5.00 provides for admission to all sessions of the Congress.

Hospital residents, interns, and medical students will be admitted without charge, if a statement of their position, signed by an official of the hospital or school is presented at the registration desk.

**MEETING PLACE:**

All sessions will be held in the Mary S. Harkness Memorial Auditorium in the Sterling Hall of Medicine at the Yale-New Haven Medical Center. The entrance is at 333 Cedar Street. This comfortable auditorium will accommodate an audience of 450.

**TELEPHONE:**

Telephone messages will be received at New Haven 562-1161, Extension 440.

**LUNCHEON:**

Luncheon for visiting physicians will be available in the Memorial Unit Cafeteria.

**PARKING:**

There are pay parking areas for visitors adjacent to the Oak Street Connector between York Street and Park Street, behind the Memorial Unit, and also on Howard Avenue.

The Yale-New Haven Medical Center is about one-half mile west of the New Haven Green. It is easily reached from the Connecticut Turnpike (via Exit 47) or from Wilbur Cross (via Exit 61) or Merritt Parkway (via Exit 57).

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**This program is dedicated to the memory of John C. Leonard, M.D. (1903-1966) late Director of Medical Education at the Hartford Hospital and Clinical Professor of Medicine at the Yale University School of Medicine, who for many years was an active member of the Connecticut State Medical Society's Committee on Postgraduate Education and a leading figure in the field of postgraduate education in Connecticut as well as nationally.**

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## PROGRAM

WEDNESDAY, SEPTEMBER 28, 1966

MARY S. HARKNESS MEMORIAL AUDITORIUM

9:00 REGISTRATION

(Coffee will be served until 9:30)

### Morning Session

9:45 WELCOME AND OPENING REMARKS

Orvan W. Hess, *New Haven, President, Connecticut State Medical Society*

#### RECENT ADVANCES IN DIAGNOSIS AND MANAGEMENT OF LIVER DISEASE

Gerald Klatskin, *New Haven, presiding*

10:00 DIAGNOSTIC PROCEDURES

WILLIAM A. TISDALE, *Burlington, Vermont; Professor and Chairman, Department of Medicine, University of Vermont College of Medicine; Chief of Medical Services, University of Vermont Affiliated Hospitals*

10:30 SURGICAL MANAGEMENT

LOUIS M. ROUSSELOT, *New York City; Professor of Clinical Surgery, New York University School of Medicine; Director of Surgery, St. Vincent's Hospital and Medical Center of New York*

11:00 PANEL DISCUSSION AND QUESTIONS

Moderator: GERALD KLATSKIN, *New Haven; David Paige Smith Professor of Medicine, Yale University School of Medicine; Attending Physician, Yale-New Haven Hospital*

Panelists: WILLIAM A. TISDALE, LOUIS M. ROUSSELOT

11:45 INTERMISSION

12:00 CLINICAL PATHOLOGICAL CONFERENCE

Presiding: PHILIP K. BONDY, *New Haven; Professor and Chairman, Department of Medicine, Yale University School of Medicine; Chief of Medical Service, Yale-New Haven Hospital*

Pathologist: AVERILL A. LIEBOW, *New Haven; Professor of Pathology, Yale University School of Medicine; Pathologist-in-Chief, Yale-New Haven Hospital*

Radiologist: ARTHUR R. CLEMETT, *New Haven; Associate Professor of Radiology, Yale University School of Medicine*

Discussant: GERALD KLATSKIN

1:00 LUNCHEON

### Afternoon Session

#### RECENT ADVANCES IN DIAGNOSIS AND MANAGEMENT OF THROMBOEMBOLISM

Stephen B. Sulavik, *New Haven, presiding*

2:30 PROBLEMS OF DIAGNOSIS

ARTHUR A. SASAHARA, *West Roxbury, Massachusetts; Clinical Associate in Medicine, Harvard Medical School; Assistant Chief of Medical Service, VA Hospital*

3:00 MEDICAL MANAGEMENT

MYRON STEIN, *Providence, Rhode Island; Director, Division of Pulmonary Disease, Rhode Island Hospital; Associate Professor of Medicine, Brown University*

3:30 SURGICAL MANAGEMENT

RALPH A. DETERLING, JR., *Boston, Massachusetts; Professor and Chairman, Department of Surgery, Tufts University School of Medicine; Surgeon-in-Chief, New England Center Hospitals*

4:00 PANEL DISCUSSION AND QUESTIONS

Moderator: STEPHEN B. SULAVIK, *New Haven; Assistant Professor of Medicine, Yale University School of Medicine; Director, Winchester Chest Clinics, Yale-New Haven Hospital*

Panelists: ARTHUR A. SASAHARA, MYRON STEIN, RALPH A. DETERLING, JR.



## Breast-feeding and the “modern mother”

Despite a mild resurgence of interest in the importance of breast-feeding a few years ago, many women today do not choose to nurse their young. This is for a variety of reasons—social, economic, cultural and sometimes medical. In such cases the physician's task is to find the most suitable means of preventing lactation and easing the pain of breast engorgement.

### The means of therapy

The value of hormone therapy for this indication is of course well established. Both androgen and estrogen are known to inhibit the production and secretion of the lactogenic hormone by the anterior pituitary. As estrogen levels decline sharply at parturition, lactogenesis is established. When androgen and estrogen are administered to the patient before the release of the lactogenic hormone lactation and breast engorgement are usually prevented.

### The time of therapy

The time of administration of this combined medication is crucial; it must be given early enough to suppress the pituitary prolactin and last long enough to permit physiologic readjustment during the puerperium. Excellent results are most often seen when therapy is administered before the onset of the second stage of labor.

However, factors other than effectiveness must also be considered. The agent selected should not interfere in any way with parturition, subsequent uterine involution and the restoration of normal ovarian cyclic function. Furthermore, it should not cause rebound breast engorgement or other manifestations of hormonal imbalance.

### A balanced formulation

Providing single-dose therapy for the prevention of lactation and breast engorgement, Deladumone OB is a potent androgen-estrogen combination with a prolonged action. The optimal balance of androgenic and estrogenic hormones achieved in this preparation minimizes the disadvantages inherent in single hormone therapy, such as rebound breast engorgement. Involution of the uterus and resumption of menstrual cycles are not affected.

As reported in a recent published study (Roser, D. M.: *Obstet. & Gynec.* 27:73, 1966), Deladumone OB provided good suppression of breast engorgement in 95.3% and suppression of lactation in 81.1% of 86 obstetrical patients. These results are in general agreement with those of many earlier investigations; in several studies this injectable androgen-estrogen combination proved to be superior to oral medication.

### Dosage:

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### Precautions and Side Effects:

Certain patients may be unusually responsive to either estrogenic or androgenic therapy. In such individuals virilization, uterine bleeding or mastodynia may occur.

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Deladumone OB, providing 180 mg. testosterone enanthate and 8 mg. estradiol valerate per cc., is available in 2 cc. Unimatic® disposable syringes and in 2 cc. vials. Both preparations are dissolved in sesame oil, with 2% benzyl alcohol as a preservative. *Before use, consult product literature for full prescribing information.*

## Deladumone® OB

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**Single-dose injection for lactation inhibition**

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# The Intensive Care Syndrome

## The Definition, Treatment And Prevention Of A New "Disease Of Medical Progress"

F. Patrick McKegney, M.D., Guest Editor

■ In his editorial in *CONNECTICUT MEDICINE* in November 1965<sup>1</sup> Doctor Louis Nahum suggests that the "madness" observed in the recovery room should be considered a new "disease of medical progress." He emphasizes the relationship, suggested both experimentally and clinically, between sleep or dream deprivation and psychotic behavior. This paper will attempt a more complete review of this topic, including some recently published material on "madness" in intensive care units. Certain factors, many of them correctable, clearly are of major significance in the development of the psychological and behavioral disturbances which are arising more frequently as increased numbers of cardiovascular recovery rooms, coronary care units, chronic dialysis facilities and other intensive treatment programs are developed. These etiologic factors will be considered in three somewhat artificially separated categories: the patient, the treatment and the setting.

An actual case vignette of operative and recovery room madness may serve to illustrate the subsequent discussion of these categories of factors.

Miss B., an 80 year old, single, retired bookkeeper, was in "good health" except for severe cataracts. Admitted for cataract removal, she was given 100 mgm. of secobarbital for sleep the night prior to operation. The next morning, she received 100 mgm. of meperidine and 100 mgm. of secobarbital as preoperative medications and the surgery was carried out under local anesthesia. During the latter stages of the operation she became very agitated and demanded to be released; her resulting physical activity severely compromised the condition of her eye. Another 100 mgm. of barbiturate intravenously did little to quiet her and four people were required to control her confused thrashing. She was taken to the recovery room with both eyes patched, and her agitation became even more pronounced. She was hallucinating voices and screaming that people were trying to kill her. A treatment regimen which included heavy doses of phenothiazine, transfer from the recovery room to her ward bed, unpatching one eye, surrounding her with familiar stimuli such as her favorite "red" radio and family pictures, and frequent contact with the nurses, produced a rapid calming effect. Two days post-operatively, she was a quiet and pleasant woman who was in grave danger of losing the operated eye. She showed evidence of a chronic brain syndrome which had existed pre-operatively but there was no residual of the acute brain syndrome with its accompanying agitation and paranoid ideation.

### Patient Factors

Each person bears physical illness in a very individual manner and his particular type of adaption to such stress seems to have implications for operative and post-operative recovery, distress or death. Throughout medical history, clinicians have been impressed that a patient who "keeps fighting" is more likely to get well. Conversely, "giving-up" seems to predispose an individual to death, even without apparent physical illness.<sup>2</sup> More recently, Blachly and Starr<sup>3</sup> noted the "surprising finding that preoperative psychiatric disturbance was related to operative mortality, an effect separate from the occurrence of a post-operative organic brain syndrome. In Abram's study,<sup>4</sup> patients who manifested denial or full-blown anxiety pre-operatively had an increased incidence of post-operative mortality and psychosis. As our treatment of formerly rapidly fatal illnesses becomes more successful, patients are exposed to a much longer course of pain, restraint, uncertainty and general emotional distress. This increase and prolongation of psychological stress forces patients to use more primitive and maladaptive coping mechanisms.<sup>4</sup> Hence, there is a predictable increased incidence of the syndromes of severe personality decompensation such as paranoid agitation or profound depression.

In addition, as the population of older persons grows, medicine is more obligated to treat and to preserve life in the aged and medically complicated patient. Thus, the more familiar factors in psychological disturbance—the patient's personality, his anxiety about illness and its implications and his repertoire of mechanisms for handling stress—are compounded by the effects of chronic brain disease and multiple illnesses which may contribute to brain dysfunction. Several authors have noted that many of the behavioral disturbances which occur post-operatively in recovery rooms have the distinct characteristics of an acute brain syndrome or "delirium": disorientation, memory defects and diffi-

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DR. F. PATRICK MCKEGNEY, Assistant Professor of Psychiatry and Medicine, Yale University School of Medicine; Chief, Psychiatric Consultation—Liaison Service, Yale-New Haven Medical Center.

culties in attention and concentration.<sup>3,5,6</sup> The severity of this delirium and its attendant behavioral disturbance has been related to the degree of seriousness of pre-operative illness. In patients with valvular heart disease, for example, the greater the degree of pre-operative cardiac decompensation, the more frequent and severe was the post-operative "complication" of a confusional psychosis.<sup>3,5</sup> Similarly, it has been demonstrated that most illnesses requiring intensive care, including renal failure, myocardial infarction or chronic lung disease, are also associated with abnormalities of brain function due to azotemia, anoxia or hypercapnia, which cause an organic brain syndrome and behavioral "complications."<sup>7</sup>

Finally, the pre-existing or baseline level of brain function is an important factor in the patient's potential for post-operative or intensive-care unit "madness." In Miss B.'s case, it is likely that pre-operatively she had a mild, chronic brain syndrome of the arteriosclerotic or senile type. Although she had been able to manage independently with these cognitive deficits, and to appear normal to the physician's casual examination, her decreased level of cerebral function was, in retrospect, a clearly predisposing factor in her operative recovery room psychosis.

Thus, the patient's psychological make-up and the brain dysfunction caused by age, by the illness which brings the patient to treatment or by other diseases, may significantly contribute to the "intensive-care syndrome". For a more comprehensive understanding of its etiology, however, factors beyond the patient and his illnesses must be considered. The treatment procedures themselves and the setting in which they are carried out can be potent causes of the "madness" of intensive-care situations.

#### **Treatment Factors**

Miss B.'s mild chronic brain syndrome predisposed her to suffer the so-called paradoxical or "idiosyncratic" reaction to barbiturates and/or narcotics. Characterized by confusion and agitation, rather than the usual desired sedative effect of these agents, this phenomenon is well recognized in children and old people. It is probably due to these drugs' selectively altering the critical balance of certain inhibitory and excitatory brain-stem centers. While this untoward reaction is both common and serious, it is not the only possible adverse sequela of medical or surgical treatment.

Both Kornfeld et al<sup>5</sup> and Blachly and Starr<sup>3</sup> noted the direct correlation between increased anesthesia time and the incidence of post-operative psychosis, reaching a frequency of 75 per cent in patients who were anesthetized for more than eight to ten hours. A similar incidence was noted in patients on cardiac

"by-pass" for four or more hours. Many operative factors such as "pump-time," number of blood transfusions, and duration of hypothermia or anesthesia tend to increase concomitantly and each has an independent deranging effect on brain function. Thus, the greater the magnitude of each of these variables, the greater the cumulative compromise of the central nervous system, and the more severe will be the post-procedure disturbance of behavior. The disorganizing effect of sleep deprivation, so common in intensive medical treatment, has been emphasized by Nahum.<sup>1</sup>

Specific studies of the effects on the brain of other variables such as the duration of use of mechanical respirators or of vaso-pressor agents, and the frequency of hemo-or peritoneal dialyses remain to be done. However, it is likely that the magnitude of artificial assistance, irrespective of type, is directly related to the degree of general central nervous derangement and, thus, directly related to the frequency of psychological and behavioral disturbances. The scope of this problem can be appreciated when one considers how much is known about nervous system disturbances associated with the common electrolyte or metabolic abnormalities such as hyponatremia, hypoglycemia, hyperkalemia, hypocalcemia, uremia or even hypomagnesemia. How many other elements of the "milieu interieur" are critically unbalanced by medical or surgical treatment methods, with resulting changes in brain function and behavior?

As complicated as the process already outlined seems to be, it is still incomplete to regard only the patient, his personality and illnesses, and the effects of medical treatment in the causation of this "intensive care syndrome". We must also consider the etiologic significance of the environment in which the patient stays and his treatment takes place.

#### **Environmental Factors**

Most recovery rooms or intensive care units are windowless, impersonal, highly mechanized, unfamiliar and isolated from the general life experience of the average patient and, thus, are potentially anxiety-provoking. More specifically, these settings are characterized by the presence of the many strange and obtrusive auditory and visual stimuli produced by oxygen equipment, monitoring apparatus, fans, respirators, air-mattresses and treatment personnel. The patient usually lies prone, in considerable pain or discomfort, almost always prevented from moving freely by apparatus or restraints, and is constantly bombarded by such stimuli, for many days without interruption, to the near exclusion of familiar sights and sounds. All of these situational characteristics are very similar to those which have been used experi-



mentally to produce psychotic behavior or to induce attitude changes in "brain-washing" techniques.<sup>8</sup> Thus, in such an environment, disorientation and psychological disequilibrium should be expected as the rule and not the exception.

Kornfeld et al<sup>5</sup> consider sensory deprivation-overload and sleep deprivation to be major factors in the psychiatric complications in the recovery-room situation. Certainly, a large body of experimental literature attests to the disrupting influence of sensory isolation and stimulus "depatterning" or overload. As one patient recently described her reaction to a prolonged operation under local anesthesia, "I kept looking at those green walls and I thought I had been swallowed by a ceramic frog."

Finally, the case of Miss B. illustrates the finding that familiar or personally significant sensory input may counteract the adverse influence of strange, impersonal or mechanical surroundings. Most people have had the experience of becoming anxious, doubtful and inadequate when driving along a road which seems totally foreign. The sight of a familiar gas station or a street sign evokes a sense of relief, increased confidence and competence. Without such reassurance, drivers have been known to stop, refusing to go any further without additional directions. The patient in the intensive care unit cannot "stop" but rather can, and does, develop bizarre modes of behavior in response to being "completely lost".

### Treatment And Prevention

These two aspects should be considered together since, as the old adage suggests, "the best treatment is prevention". The most important single element in prevention is the physician: his awareness of the contributing factors outlined above, his eliminating or minimizing as many as possible and his anticipation and early recognition of their possible consequences. If the physician is assisted in these tasks by a treatment team—a "team" in the true sense of the word—the "intensive care syndrome" should become an infrequent problem. Measures to achieve this goal must become the responsibility of not only the physician, his medical assistants, the nursing personnel, and social service but of the hospital administration as well.

The physician's relationship with his patient has been recognized as generally useful from time immemorial. More specifically, recent evidence supports the efficacy of doctor-patient rapport in reducing post-operative pain.<sup>9</sup> A close relationship will afford the physician more information about the patient's personality, his capacities for handling stress and his baseline level of brain function. Furthermore, the patient will be able to rely more effectively upon the physician with whom he has a firmly established relationship.<sup>4</sup> It is apparent that

all of these effects of a good doctor-patient relationship are specific antidotes for some of the causes of the "intensive care syndrome".

Also of importance in the prevention of this syndrome is the physician's ability to familiarize his patient with the illness and the modalities of the proposed treatment. The value of a patient's learning about such matters, including visiting the site of future treatment, has been recognized in modern obstetrical care. This approach is even more applicable in situations in which the illness is more life threatening, the treatment setting more complex and stressful, and treatment outcome more uncertain, than in a normal pregnancy. The patient's meeting with the nursing and medical personnel prior to admission can increase the patient's trust in those caring for him at the time of crisis, diminishing his feelings of unfamiliarity or isolation, and improving his psychological homeostasis.

In certain instances, however, this pre-acquaintance is obviously not possible and more emphasis must be placed on other techniques. Many of these have been outlined in the paper by Kornfeld et al,<sup>5</sup> which suggests presenting the patient with a variety of simple, structured stimuli, eliminating exposure to sights and sounds such as paging systems, respirators or other patients' sufferings or treatments. Many other characteristics of the intensive care setting, for example the absence of windows, natural light or diurnal variations of surroundings, should also be corrected whenever possible.

Another important facet of intensive care, which must be considered in some depth, is the use and abuse of monitoring or treatment equipment. Kornfeld et al suggest that such instruments be kept beyond a patient's perceptions, to reduce stimulus monotony and patient anxiety. However, of greater significance regarding such equipment is the fact that medical personnel often rely to an inordinate degree upon cardiac monitors, pacemakers and other apparatus. No mechanical device or pharmacological treatment has yet been devised which adequately substitutes for human observation or, more importantly, for human, personal attention to a distressed patient. A recent case of a 65 year old man with a myocardial infarction, ventricular bradycardia and hypotension illustrates this point. An intravenous Isuprel drip maintained a normal rhythm and blood pressure, which was observed with a cardiac monitor placed in the hall outside the patient's room. The very busy nurses could easily check the monitor constantly, though they actually visited the patient infrequently. Around midnight the cardiac monitor alarm indicated the patient had suffered a cardiac arrest. Cardiac massage produced a prompt resumption of a ventricular bradycardia and it was realized that the

Isuprel infusion had run dry. Because of the patients now precarious state, an intravenous cardiac pacemaker was inserted, and the patient's recovery was prolonged, complicated and threatened by this incident.

The labor-saving benefits of telemetering devices or "efficient" floor plans can be deadly traps. What may be most economical in terms of low ratios of nurses to patients may not be consistent with optimal patient care or with prevention of the intensive care syndrome.

Another aspect of the intensive care problem is that of staff reaction and function. An approach to the personnel problems in the intensive care unit is described in Koumans' article.<sup>6</sup> He recognizes the special nature of such a unit, which results from the high percentage of seriously ill patients, their short term stay and the highly complex set of duties required of the staff. He recommends providing emotional support to treatment personnel, developing a team operation, and ensuring a stability of personnel assignments in order to offset these special stresses in intensive care units. To compensate for the serious nursing shortage many resources can be tapped. Using responsible family members, social workers, chaplains, volunteer workers, and other community resources to provide close personal contact with the patient can be of major value in avoiding the "intensive care syndrome."

Finally, it is apparent that minimizing the physiological stresses due to premedication, analgesia-sedation and duration of anesthesia, by-pass and hypothermia, will decrease the incidence of delirium in intensive treatment patients. Phenothiazines, which do not disorganize cognitive functions to the same degree as barbiturates or narcotics, can potentiate and lower the requirements for these latter agents, with resultant lessening of confusion and agitation.

## Summary

The "intensive care syndrome" is a new disease of medical progress, manifesting itself in a variety of newly developed treatment situations. The etiology of this syndrome can be conceptualized as a composite of many factors including: the patient's personality, illnesses which affect the patient and his organic brain function, the effects of the treatment regimen and the influence of the setting in which treatment takes place. Prevention and treatment of the syndrome requires the physician's being aware of these factors and instituting measures to minimize them. The development of a treatment "team" and the organization of the treatment environment is considered crucial in controlling the "intensive care syndrome".

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Hilarity and good humour, a breezy cheerfulness, a nature "sloping toward the southern side," as Lowell has it, help enormously both in the study and in the practice of medicine.

—Sir William Osler



# Child Psychiatry In Relation To The Community And Its Facilities

Melvin Lewis, M.B., B.S., D.C.H. and Laura Codling, A.C.S.W.

■ Child psychiatry is a medical specialty concerned with promoting the healthy psychological development of the child. Throughout his development the child is confronted with life tasks that often give rise to varying degrees of discomfort. The services of child psychiatrists are frequently sought toward understanding and alleviating such discomfort insofar as it interferes with the progressive development of the child. However, by no means do all such discomforts require the skills of a child psychiatrist, nor is the work of the child psychiatrist confined only to direct therapeutic intervention with the child and his family in isolation from the community and its facilities. Indeed, much important preventive and therapeutic assistance is given by allied professions before, during, and after consultation, evaluation, and treatment by the child psychiatrist. Our purpose here is to describe some of the relationships between child psychiatry, the child and his family, and the facilities in the community.

The physician is first faced with the task of defining who is making the complaint, whether it is the child who is the true object of the complaint, and what exactly is the nature of the complaint. It is not always the child who is the "problem." While a parent may complain that his child is upset, or in trouble, or causing the parent distress, this may not be the actual motivation for the parents' seeking help. A parent, for example, may be motivated by a court order, or a desire to establish a case for (or against) a custody proceeding, or by outside social pressure exerted by other agencies, the school, neighbors, or other members of the family. The degree of this outside social pressure is in turn related in part to the tolerance of the individual concerned, whether teacher, neighbor, or other family member. Conversely, parents may be using the child as a ticket of admission in seeking help for their own personal problems.

Children themselves rarely directly verbalize their need for help, but do frequently demonstrate their discomfort in their behavior. This behavior may or may not cause discomfort to the parents. Certainly the description of the child's behavior as given by the parents is not always in accord with that given by other observers, nor is the actual degree of discomfort in the child always correctly assessed. Sometimes the behavior of the child is labelled in such

a way as to imply a diagnosis which may not in fact be the case. For example, the presenting complaint may be that of "temper tantrums," implying a discharge of aggression. Further study, however, may reveal a diagnosis of psychomotor epilepsy, or behavior resulting from overwhelming anxiety.

In child psychiatry the assessment of the development of the child in terms of normality is of course complex and beyond the scope of this paper. The basis of our knowledge about the psychological development of the child is derived from many fields, including psychoanalysis, child development, education, child psychology, anthropology, and pediatrics. The psychoanalytic theory of personality development is especially useful in understanding the development of the child, and provides a practical framework within which a developmental profile of the child may be drawn.<sup>1</sup>

The principal method of study is the clinical interview. Psychological tests and other special studies provide further information. Primary data is obtained first of all from a comprehensive pediatric history. An assessment is next made of the state of drive development and distribution, and the development of psychic structures in the child. A clinical picture of the various lines of adaptive development is sought. These lines include the development of relationships, various expressions of the degree of achievement of body independence (such as attitudes to eating, autonomous control of bladder and bowel functions, and proper individual health care), the capacity to enjoy other children, and the ability to play and work. The child psychiatrist looks for significant regressions and fixation points, and the nature of the psychological conflicts that are present. Certain general characteristics such as the child's frustration tolerance, his capacity for sublimation, the child's response to anxiety and the balance of forces which determine the tendencies in the child toward progression or regression are also noted.

On the basis of such an assessment it is possible to arrive at a diagnosis of the psychological develop-

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ment of the child. For present purposes the following broad diagnostic classification, based on Anna Freud's work, will enable us to consider the treatment needs of the child, and the relationships between the child psychiatrist and the community and its facilities in meeting these needs:

1. Variation of normality.
2. Transitory symptoms as by-products of developmental strain.
3. Neurotic conflicts leading to childhood neuroses and character disorder.
4. Severe regressions, leading to infantile behavior, borderline, delinquent, or psychotic disturbances.
5. Certain primary deficiencies of an organic nature, or early deprivations which distort personality development, leading to retarded, defective, and non-typical personalities.
6. Those children in whom destructive processes, e.g. organic, toxic or psychic, known or unknown, are at work.

Clearly in some instances, e.g. when the behavior represents a variation of normality, or a transitory symptom produced by temporary imbalance between the child's maturation, functional capacities and environmental support, helpful guidance by an understanding person may be all that is required to prevent the occurrence of psychological disorders and encourage healthy development. Such help is well within the skills of a wide range of professional personnel, including family doctors, pediatricians, school guidance personnel, teachers, and public health nurses. Child psychiatry can offer indirect help in the form of consultation to such professional personnel to help them enhance their particular skills.

Where childhood neuroses or character disorders have developed, some form of direct psychiatric treatment is usually indicated. The core of such treatment in child psychiatry is some form of psychotherapy. Treatment on a weekly or more frequent basis, either individual or in groups, involving the parents as well as the child, may extend from a period of a few months in some cases to years in others.

Sometimes the disorder is more severe, as in certain borderline and psychotic disturbances. More intensive treatment is needed, particularly in the area of more control of the child's environment. Various inpatient settings are then indicated.

Within some communities there are agencies which offer both direct and indirect kinds of psychological help in each of the diagnostic categories mentioned. Many communities have only limited facilities and can only offer an attenuated form of indirect help. The child psychiatrist may participate, in varying degrees, in both the direct and

indirect help to the psychological well being of the child and his family, within the context of one or more of the agencies present in the community. Accordingly, for purposes of discussion, we will describe certain typical community agencies concerned with the progressive psychological development of the child within the two broad groups, designated as mainly "direct" and mainly "indirect," recognizing of course that many agencies offer both kinds of service. The role of the child psychiatrist in relation to these agencies will be discussed.

### **Direct Services**

The three major types of direct child psychiatric service include outpatient clinics, residential treatment centers, and hospital ward facilities.

#### **a) PSYCHIATRIC OUTPATIENT CLINICS FOR CHILDREN**

Children who fall into almost all of the diagnostic categories may benefit in some degree from outpatient treatment. The criteria for outpatient help lie more within such areas as the degree to which the child's conflicts are internalized and amenable to psychotherapy and the extent to which the environment of the child can be modified through guidance and treatment offered to the parents, rather than the specific diagnosis. Generally, however, most children who receive direct treatment at child guidance clinics fall within the categories of the neurotic disturbances and character disorders. The actual type of disorder varies according to the development level of the child. For example, the preschool child may have various kinds of sleep disturbances, persistent wetting and soiling, and difficulties in tolerating any degree of separation. The school age child may have a school learning difficulty, or may have developed a phobia or a behavior disturbance. During adolescence, problems around such developmental tasks as identity, body and instinctual mastery, and relationships with parents may give rise to a wide variety of neurotic symptoms and behavior disturbances.

Curiously, most psychiatric outpatient clinics for children see more boys than girls. This partly reflects the greater frequency among boys of some conditions, e.g. enuresis, stuttering, tics, certain kinds of reading difficulties, fire setting, etc. In addition, the degree of a behavior disorder in boys is more likely to exceed the tolerance of the family or community, leading to a greater frequency in referral to a child guidance clinic.

The prototype for outpatient psychiatric help for children in the community is the child guidance clinic. Usually the staff of such clinics consists of a child psychiatrist as director, a social worker, and a clinical psychologist. Many clinics have additional full or part-time staff in each of these disciplines, and utilize additional facilities within the com-



munity both for special diagnostic and collaborative therapeutic work. Thus the pediatrician, visiting nurse, welfare worker, school personnel, etc. may be actively involved. The range of treatment offered may include individual psychotherapy for the child, group therapy, parallel treatment of a parent and child, and many more. Various members of the child guidance clinic may conduct the therapy. Furthermore, the child guidance clinic may activate a wide variety of community resources to provide additional help to the child and his family, e.g. special help in school, VNA, homemaker service, foster home placement, protective services, etc.

In referring a family to a child guidance clinic, consideration should be given to the preparation of the family. Members of the family may have many questions and expectations concerning psychiatric treatment. The referring person can be of considerable help to the family by allaying their fears and providing them with a realistic account of what they can expect. The child psychiatrist can be of help to the referring person in the matter of such preparation.

In addition to their direct services, many child guidance clinics offer consultation services to various community agencies and facilities, e.g. schools, Juvenile Courts, the Visiting Nurse Association, and many others. This type of service will be discussed shortly.

Some outpatient psychiatric clinics for children in Connecticut are a part of a hospital or medical center, while others have been established independently in communities, under voluntary auspices. All clinics to be recognized as community psychiatric services must meet minimum standards established by the Division of Community Services of the State Department of Mental Health. Some of the clinics, in addition, have met the standards and are members of the American Association of Psychiatric Clinics for Children. This is a national association of child guidance clinics that was established in the 1940's, with one of its purposes being the setting of standards for psychiatric clinics and qualifications for personnel in the field of mental health for children. It also sets standards for training programs and for clinics approved as training clinics for child psychiatrists.

Problems of financial support for the maintenance of services is a complex one for most child psychiatry clinics. Many clinics have developed multiple sources for financial support. Some clinics may depend on one or more community resources such as United Funds, private foundations and voluntary contributions, as well as state, federal, or local public funds. Adequate financial support is an important factor in defining for most clinics the extent of services they are able to provide, although

not of course the only factor.\* Additional funds necessary for the expansion of outpatient psychiatric services for children has not kept pace with the increasing demand for such services. Available services are limited and most clinics have extensive waiting lists, especially for those problems requiring intensive or extended psychiatric treatment. Brief psychiatric evaluation and/or consultation is more readily available. However, even if there were unlimited funds, the shortage of trained child psychiatrists that would still exist would continue to impose limitations on the amount and kind of services offered.

#### **b) RESIDENTIAL TREATMENT CENTERS**

Certain children need a more structured setting for their treatment. Some of the signs that might indicate this need include repeated and sometimes dangerous anti-social acts, such as firesetting, stealing, and assaultive and destructive behavior. Most of these children have severe school learning difficulties, and some may have been expelled from school. They rarely have good relationships with either adults or peers. Sometimes there is a history of many foster home placements, or severely disorganized families now threatened with further stress, e.g. illness, desertion, death, etc. Sometimes a markedly atypical child in a normal family requires the aid of structured environment that the family cannot provide in their home.

Various residential treatment centers have developed programs to meet the needs of certain groups of these emotionally disturbed children. The programs usually provide individual therapy to the child and help to their families, special small classes or individual teaching if needed, and a group living experience that provides them with the support and rules they need as well as the constant expectation of achievement. The staff of such residential treatment homes accordingly include child psychiatrists, social workers, teachers, child care workers, pediatricians, psychologists, and workers in arts and crafts.

Each center has developed its own program, and careful screening procedures are used to insure that their program is likely to benefit the child.† Again, boys seem to be more frequently referred for residential treatment than girls.

In developing their programs, these residential treatment homes have made special efforts to remain in touch with their related communities. Local schools and recreation facilities (e.g.

\* For further details of the extent of the services offered by a particular child guidance clinic, that clinic should be contacted directly. See Appendix I.

† For further details of their intake policies, screening procedures, and treatment programs, it is advisable to contact directly the individual center. See Appendix II.

Y.M.C.A.) may have a significant part in their programs. Often liaison with workers from other community and state agencies, e.g. local welfare departments, Division of Crippled Children, Division of Child Welfare, Aid to Dependent Children, is necessary in the treatment of a family who has a child member in a residential treatment home.

#### **c) HOSPITAL FACILITIES**

In some instances the child will require diagnostic and intensive treatment facilities within a protective environment of a hospital ward. In nearly every instance a severe failure in adaptation has occurred. The manifestations of such a failure often present as clinical pictures that fall within the categories of severe neurosis or acting-out character disorders; massive regression leading to borderline, delinquent, or acute psychotic disturbances; severe atypical development; and acute or chronic organic disorders. For example, in infancy the clinical picture may be that of an acute failure to thrive. Another clinical picture may include such symptoms as an inability to relate, obsessive desire for the maintenance of sameness, disturbances of language development (e.g. muteness, echolalia, confusion of personal pronouns), panic stricken behavior and bizarre postures, constituting the syndrome of infantile psychosis. In other children, conversion symptoms such as blindness, astasia-abasia, and convulsive-like behavior may occur. During adolescence, a severe failure of adaptation may manifest itself in a suicidal attempt, with an underlying acting-out character disorder or schizophrenic reaction.

Three types of hospital ward facilities are currently available for the management of these and similar conditions: psychiatric wards for children (The Children's Unit of Connecticut Valley Hospital), mixed psychiatric wards in psychiatric or general hospitals, and non-psychiatric (usually pediatric) wards in general hospitals.

#### **The Psychiatric Ward For Children**

At present, the Children's Unit at the Connecticut Valley Hospital, a state institution, is the only hospital facility in the state that offers psychiatric diagnostic and treatment facilities exclusively for children who are severely disturbed. The Unit itself is constantly attempting to improve its services.

As it is presently constructed, the Children's Unit consists in essence of one ward for boys and one ward for girls, housing a total of approximately 65 or more children. The hospital is relatively isolated, of course, from most communities in the state, so that most parents cannot attend regularly, and contact is maintained mostly by telephone. The Unit tries to work closely with local community agencies.

The ward environment and therapy is at present in the charge of a social worker acting as head of the Unit. Attempts have been made to devise special programs for certain groups of children, e.g. autistic children. Child psychiatry consultants supervise and teach. At the time of writing, none of the actual psychotherapy of the children was done by child psychiatrists. An on-grounds school is included in the treatment program.

The Children's Unit is an important resource in that it is the only psychiatric ward in the state exclusively available for children, and one that also serves every community in the state. Children who are in need of a protective environment where a diagnostic evaluation and treatment plan can be devised, and for whom no other resource is available, may be referred to the Children's Unit. It should be noted, however, that the Children's Unit has established its own intake policies and procedures, and will not admit a child unless the staff consider it clearly indicated, or, as stated by law, the child is a danger to himself or others.

#### **Psychiatric Ward In A General Hospital**

Where they exist, the psychiatric wards in some private psychiatric hospitals and in certain general hospitals are often able to admit children, depending on their patient population and available staff. Usually such wards can admit children in the latency and adolescence stage of development, who need psychiatric evaluation and who are likely to benefit from a relatively brief period of intense treatment in which the ward environment is a major force. Child psychiatry consultation and supervision is often available, although the direct work with the child and his family is usually carried out by the regular psychiatric, social work, and nursing staff of the ward. Admission to such facilities is of course solely the prerogative of the ward admitting staff.

#### **Non-Psychiatric (Pediatric) Wards In General Hospitals**

The pediatric ward is unique in that it is the one inpatient setting that can actually offer the opportunities for the enhancement of psychological development and the prevention of psychological disturbance, as well as the care of the emotionally ill child, through the collaborative effort of pediatrician and child psychiatrist. The assistance offered through careful preparation and suitable modification of the ward environment may help a child and his family as the child encounters a developmental (life) task during his hospitalization for medical or surgical purposes. The resolution of such major tasks of childhood as separation, body image and identity formation, and mastery of instinctual drives



may actually be facilitated, particularly in the case of older children.

The prevention of psychological disturbance that may arise when the child has the kind of illness that may threaten the psychological health of the parent-child relationship, or may traumatize the child, can also be effectively carried out through collaborative care between pediatrician and child psychiatrist on a pediatric ward.

In some instances the pediatric ward provides a suitable environment for the initial management of an acute psychological crisis, e.g. failure to thrive or child abuse due to disturbed parent-child relations, acute exacerbation of a so-called psychosomatic disorder, and some instances of attempted suicide in adolescence.

The effective adaptation of the pediatric ward for the management of these conditions depends upon a number of factors. For example, the attitude and understanding of the pediatrician in dealing with psychological disorders of childhood often determines whether such work can be accomplished. Also, the ward environment, which includes the patient population at any given time, the presence of adequate nursing staff, and the availability of a child psychiatrist, may be an important factor. The use of a pediatric ward for the management of psychological disorders in children therefore requires the constant appraisal of all these factors, an appraisal which benefits from the combined judgment of child psychiatrist, pediatrician, and nurse. For example, there are occasions in which the continued adaptation of the pediatric ward may deplete the resources of the ward personnel, running the risk then of diminishing the quality of care to the other pediatric patients as well as to the particular child for whom the adaptation was made.

### **Indirect Psychiatric Services To Children**

The child psychiatrist is of course concerned with the normal development of the child, the prevention of disturbed development, and the diagnosis and treatment of children with psychopathological conditions. At the same time it is obviously impossible for every family to have a child psychiatrist observe the development of their child and help in the countless life crises that occur with especial frequency during periods of relatively rapid change in development. Fortunately, many agencies and facilities are available to the child and his family, notably pediatric services, school facilities, family service agencies, and the whole range of socioeconomic measures offered by the Division of Child Welfare, Aid to Dependent Children, visiting nurse associations, homemaker service, and if necessary protective services. In addition, those children with special handicaps such as a birth defect, mental

retardation, cerebral palsy, deafness, blindness, and many more, have access to special services to meet some of their special needs.

The relation of child psychiatry to each of these community facilities may take a number of forms. Sometimes the relationship is that of consultation on the matter of diagnosis and management of a particular child and his family. On other occasions the child psychiatrist may be an active member in the treatment plan involved in the care of a particular child and his family. At other times the child psychiatrist is engaged in an ongoing teaching program with a particular agency. Occasionally the child psychiatrist is a participant in a multidiscipline research project. In some of these agencies the child psychiatrist performs all these functions, e.g. in relation to pediatrics, while in others of course his function is less encompassing.

The relations of child psychiatry to pediatrics and school services are particularly important. A full discussion of these relationships and their practical implications is beyond the scope of the present paper.<sup>2</sup> "Child psychiatry" here may be represented by members of the child guidance clinic other than the child psychiatrist. Thus, clinical psychologists and social workers may carry out the work presently to be described.

Knowledge and techniques in child psychiatry provide important elements in the training of the pediatrician. The areas of knowledge include: personality growth and development; interviewing techniques; child-parent-physician relationships; psychological reactions of children and parents to physical illness and convalescence; psychopathology and symptom formation. Child psychiatry also complements certain research activities, and enables the pediatrician to practice comprehensive pediatrics. *Mutatis mutandis*, child psychiatry benefits from the knowledge and techniques of modern pediatrics. Collaboration between the child psychiatrist and pediatricians in private practice, the pediatric clinic, and the pediatric ward is a *sine qua non* of modern care of children with certain kinds of problems.

Child psychiatry in relation to the school has taken a number of forms.<sup>3</sup> In the nursery school, child psychiatry can contribute knowledge of child development and parent-child relationships to the teacher who tries to provide the child with an opportunity to develop his skills and personality. In some instances a particular problem may be the focus of attention, e.g. separation anxiety, discipline, kindergarten, or school readiness. Sometimes the nursery school teacher is enabled to detect early signs of psychological distress. Here, *par excellence*, is the opportunity for primary and secondary prevention in child psychiatry.

In the elementary schools the relationship between child psychiatry and the teacher is very much a reciprocal one. The child psychiatrist learns from the teacher the academic performance and behavior of a particular child, the school's understanding of the problem, and their methods of management. By the same token, through consultation with the child psychiatrist, the principal and teacher may gain further understanding of certain children and the difficulties they and the children are experiencing. The child psychiatrist may in addition meet with a group of principals or teachers in a continuous seminar. Such seminars serve several purposes, including the development of an understanding of certain problems that children present in the classroom, ways of exploring the causes of these problems, and methods of management. Observation by the child psychiatrist of the child and teacher in the classroom setting may facilitate these purposes. Occasionally, the child psychiatrist may interview a particular child, with the consent of the parents.

In his direct work with the child, a school visit by the child psychiatrist, who has first discussed the visit with the child and his parents, may be especially helpful. Further studies and methods of management are often suggested by such exchanges.

Certain special problems, such as reading difficulties, learning inhibitions, and behavior disturbances due to a variety of causes, may require not only special study but the true collaborative services of teacher, psychologist, social worker, pediatrician, and child psychiatrist. The child psychiatrist may perform the important function of synthesizing these efforts.

Clearly, the child psychiatrist cannot perform all of these functions, nor will he be able to do so in the foreseeable future. At present in the State of Connecticut there are two training facilities for child psychiatrists: the Child Study Center, Yale University, New Haven, and the Children's Clinic of the Institute of Living in Hartford. Currently, the total number of child psychiatrists who complete their training in Connecticut rarely exceeds three a year, and has often been less. Furthermore, it is by no means certain that these child psychiatrists will stay in the state on completion of their training. Thus the rate of increase, real and apparent, of problems in the child population far exceeds the rate of training of child psychiatrists in the state.

Further, a number of important facilities are still not available in the state at the present time. Some of the needed facilities include a residential treatment home for very young children (under the age of 5 years); a special psychiatric diagnostic unit for children in immediate need of care and protection; residential treatment homes for boys over the age of 12 and girls over the age of 15 years; more out-

patient services for children, particularly for adolescents between the age of 15 and 18; day care centers for certain groups of children, e.g. the autistic child; more transitory half-way homes for rehabilitation of children back into the community after a period of residential treatment; inpatient settings within the community for the management of acute psychological disturbances in adolescence; group homes for children and adolescents who need to be out of their own homes (or who have no home) and yet do not need residential treatment although they may require outpatient help; ongoing community-based inpatient services for the intensive treatment and continuous supervision of severely disturbed children and adolescents.

Some planning for children in Connecticut has taken place, although there is as yet no published master plan. In 1963, the Community Mental Health Centers Act authorized appropriations totaling \$150 million over three fiscal years, 1965-67, enabling states to establish programs that provide at least the essential elements of comprehensive community mental health services. The five essential elements included: (1) inpatient services; (2) outpatient services; (3) partial hospitalization services such as day care, night care, weekend care; (4) emergency services 24 hours a day to be available within at least one of the first three services listed above; (5) consultation and education services available to community agencies and professional personnel. Unfortunately, services for children were not specifically defined in the Act. It is to be hoped that services for children in all these essential elements will eventually be provided.<sup>4</sup>

The unique contributions of child psychiatry lie in its study of the complexity of the development of the child and his family and its understanding of disorders of development. This contribution is kept alive by the study and treatment of the individual child and his family. Such work is the core of child psychiatry as it is practiced in the child guidance clinic.

Child psychiatry in the community is faced with the problem of priorities in exercising a number of responsibilities. Some of the responsibilities that are considered are those of training in child psychiatry, teaching in other branches of medicine, research, direct work with the individual child, and the increasing need for indirect work through the many health, education, and welfare agencies in the community concerned with the development of the child.

Local community needs, the support and cooperation of the lay and professional communities, and the skills, interests, and goals of the child psychiatry staff are important factors in determining the priorities in a given community.



But there is a still larger context for child psychiatry. In many instances the inadequate development of the child is the result of factors that extend beyond the intrinsic psychological and organic factors within the individual child and his family. Thus cultural, educational, socio-economic, and health factors play an overwhelming part in some cases. Primary prevention in child psychiatry necessitates collaboration, therefore, not only in direct and indirect intervention at the immediate community level, but in an attack on the problems involved at state and federal levels. At the present time this level of collaboration is in its earliest stages. Undoubtedly such collaboration will become more prominent in the future. Along with such collaboration, certain kinds of combined epidemiological studies may become increasingly important. The results of such studies may then lead to changes in the relationship of child psychiatry to the community and its facilities.

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APPENDIX I

*Outpatient Psychiatric Clinics for Children in Connecticut*

BRIDGEPORT

The Child Guidance Clinic of Greater Bridgeport, Inc.  
1081 Iranistan Avenue  
Bridgeport, Connecticut 06604  
Telephone: 367-5361

DERBY

The Alice Russ Cochran Psychiatric Clinic  
Griffin Hospital  
Derby, Connecticut 06418  
Telephone: 735-7421

HARTFORD

The Hartley-Salmon Child Guidance Clinic of Children's Services of Connecticut  
1680 Albany Avenue  
Hartford, Connecticut 06105  
Telephone: 236-1294  
Children's Clinic, Institute of Living  
17 Essex Street  
Hartford, Connecticut 06102  
Telephone: 525-8681

Division of Community Services  
State Department of Mental Health  
79 Elm Street  
Hartford, Connecticut 06115  
Telephone: 527-6341, Ext. 830

LAKEVILLE

Housatonic Psychiatric Center  
Lakeville, Connecticut 06039  
Telephone: 435-2529

MANCHESTER

Community Child Guidance Clinic  
317 North Main Street  
Manchester, Connecticut 06040  
Telephone: 634-2101

MERIDEN

Child Guidance Clinic for Central Connecticut, Inc.  
117 Lincoln Street  
Meriden, Connecticut 06450  
Telephone: 235-5767

NEW BRITAIN

Child Guidance Clinic, Inc.  
205 West Main Street  
New Britain, Connecticut 06052  
Telephone: 223-2778

NEW CANAAN

Community Clinic of the Silver Hill Foundation, Inc.  
Valley Road  
New Canaan, Connecticut 06840  
Telephone: 966-3561

NEW HAVEN

Clifford W. Beers Child Guidance Clinic, Inc.  
432 Temple Street  
New Haven, Connecticut 06510  
Telephone: 772-1270  
Yale University Child Study Center  
Child Psychiatry Unit  
333 Cedar Street  
New Haven, Connecticut 06510  
Telephone: 562-1161, Ext. 2140

NEW LONDON

Child Guidance Clinic of Southeastern Connecticut  
75 Granite Street  
New London, Connecticut 06320  
Telephone: 442-0319

NORWALK

Mid-Fairfield Child Guidance Center  
74 Newtown Avenue  
Norwalk, Connecticut 06851  
Telephone: 847-3891

NORWICH

The United Workers of Norwich  
Family and Children's Service  
P.O. Box 428  
Norwich, Connecticut 06360  
Telephone: 889-7353

#### STAMFORD

Psychiatric Clinic for Children, Inc.  
103 West Broad Street  
Stamford, Connecticut 06902  
Telephone: 324-6127

#### WATERBURY

Child Guidance Clinic of Waterbury, Inc.  
52 Pine Street  
Waterbury, Connecticut, 06710  
Telephone: 756-7287

### APPENDIX II

#### *Residences that also offer treatment (Residential Treatment Centers and Schools)*

##### HIGH MEADOWS

Connecticut Child Study and Treatment Home  
825 Hartford Turnpike  
Hamden, Connecticut  
Telephone: 248-4421

A residential psychiatric center for children, created by State statute. The home provides a 24 hour a day living program and therapeutic services for boys.

##### HIGHLAND HEIGHTS

651 Prospect Street  
New Haven, Connecticut  
Telephone: 777-5513

A private residential treatment home, under the auspices of the Sisters of Mercy. The home provides a 24 hour a day

living program and therapeutic services for 12 boys and 12 girls.

##### CHILDREN'S CENTER

1400 Albany Avenue  
Hartford, Connecticut  
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—Sir Thomas Browne, *Religio Medici*. Edited by W. A. Greenhill, M.D., London, MacMillan and Co., Ltd., 1950, p. 38.



# Post-Partum Depression: A Case Review Diagnostic, Treatment, And Socio-Medical Aspects

Edward C. Senay, M.D.

## Introduction

■ Post-partum emotional disturbances are frequent and range from short lived "baby blues" to full blown psychoses.<sup>1-3</sup> Decisions about the severity of such reactions are often difficult because of defensive operations on the part of patients and their families. The situation is further complicated by the fact that the medical profession, reflecting the general cultural belief that emotional symptoms in a post-partum context are expectable and transitory, tends to disregard symptoms which, in some instances, are real and desperate calls for help. Present day specialization in medicine adds further difficulties. The perceptions of the specialist's role on the part of both patient and doctor serve to structure behavior so that certain kinds of information are given to one specialist, different information is given to another, and so on.

The following case review focuses on these aspects of the disease process and summarizes the psychiatric management of the syndrome. The case history should also serve to illustrate the complexity of the patient's psychologic breakdown and to point out the inaccuracy of using the term "post-partum" depression in an etiologic sense.

## Onset And Course Of Symptoms

The patient was a twenty-seven year old white female, the wife of a professional man. Eight months prior to referral, she had given birth to her fourth child. Her immediate post-partum course had been uneventful. One month after delivery, however, she began to experience anxiety, irritability, anorexia, early morning awakening, and gastrointestinal complaints. These symptoms were mild and intermittent at the onset but over a period of weeks they became more severe and persistent. The patient began to weep frequently and to neglect her household duties. She experienced occasional terror and began to withdraw from her husband and children. She became extremely fearful of leaving her home and began to insist that everything in her house had to remain exactly where she had placed it. She could not tolerate the thought of being left alone when her husband's work called him away. She began to feel that her children belonged to someone else. Caring for her infant was

especially difficult because it induced intense panic and feelings of depersonalization. She began to ruminate about suicide. In the next few months, these symptoms worsened and one month prior to referral, she experienced auditory hallucinations.

## Patient's Defenses

The patient attributed her early symptoms to the birth of her child. She felt that her difficulties were not unusual and that she would soon recover. Feeling that catching up on sleep would return her to normalcy, she began to take afternoon naps. As her condition worsened, she utilized denial, dissociation, and withdrawal to an increasingly pathological extent. She described her least troublesome symptoms to her husband but would not admit inwardly or outwardly that she was in difficulty. Although her post-partum course in her three prior pregnancies had been uncomplicated, she insisted that her symptoms were attributable to a state of fatigue following childbirth. To maintain denial of her distress, she distorted many aspects of her pre-marital personality. She stated, for example, that her social withdrawal was due to her post-partum condition when, in fact, it had been an increasingly prominent part of her life for most of her married years.

## Response Of The Family

During the early stages of the illness, the patient's husband had joined in the patient's belief that her difficulty was attributable to post-partum fatigue. As her condition worsened, the family's attitude toward the situation did not change but they did take action. The patient's mother was summoned to live in their home. She partially sought and partially was given the patient's role to the point of having assumed, at the time of referral, all the patient's household duties while the patient remained largely confined to her room. The patient's mother joined in the belief that the trouble was the result of postpartum factors.

It is of interest to note that although they complained somewhat desperately about the worsening

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situation, all three tended to minimize and deny the severity of the patient's deterioration. They steadfastly maintained that the patient had been well adjusted prior to her present illness.

### **The Medical Community And The Illness**

The patient, and to a lesser extent, her husband, had frequent contact with the medical community during the entire course of the illness. Their description of her difficulties to various physicians can be seen as a function of their perception of the role of the physician whom they were visiting and as an attempt to deny the severity of her difficulties. For example, the patient complained to her family physician that her sinuses were bothering her; she also complained of vague gastrointestinal symptoms and fatigue. She did not describe her panic nor many of the other symptoms which were troubling her far more than those which she presented. She was told that her difficulty was common and the result of post-partum factors. In her follow-up visit to the obstetrician, she again structured her complaints so that her situation was minimized. She received reassurance that her feeling of fatigue would improve fairly rapidly.

When her symptomatology worsened, the family decided to visit an internist. By this time, the pressure had increased on all family members. Although the patient presented the same kinds of complaints to the internist that she had presented to the family practitioner, she communicated a feeling of desperation, largely by non-verbal means. The internist recognized that she was depressed and started her on antidepressants. Her response to the medication was striking. Shortly after taking her prescribed dose, she experienced a feeling of intense panic. She would feel unreal and become tearful, often withdrawing to her room. When she returned on a follow-up visit to the internist she was finally able to describe her most troublesome symptoms but she could do this only when she could attribute them to the taking of drugs. The internist realized the full extent of the patient's distress and referred her to a psychiatrist.

Her presentation to the psychiatrist was quite different than her approach to other physicians. The defensive operations of the patient and of the family were seriously impaired by their perception of a psychiatrist as one who would be able to see through them. Prior to the referral, the patient became convinced that she would never recover and would end her days in a state hospital. In the referral situation, both patient and husband were exceedingly fearful and almost mute. They presented in such a disorganized manner that the psychiatrist soon began to speak of hospitalization as a real possibility. The family interpreted his remarks to mean that

she would have to go to a state hospital and probably have to stay there for the rest of her life. The family returned to the internist in a state of panic, at which point they were referred to this center for further psychiatric consultation.

### **Initial Work Up**

When seen here, they again presented in a disorganized fashion. The patient was nearly mute and the husband was quite anxious. A question at that time was: How much of their present behavior was a function of the situation they were in and how much was a function of the disease process? They were invited to discuss all of their problems and were assured that extra time would be spent in reviewing their situation in detail. Slowly, over the course of the initial session, they began to relax and the true level of difficulty emerged. They were seen at another hour later in the day for further discussion and review. The question of hospitalization could then be discussed realistically. A judgement was made that there was enough support in the patient's family to enable her to remain at home and to be treated as an outpatient.

On the following day, the patient's mother was seen individually and together with the patient and her husband. A total of 6 hours was spent by the psychiatrist with this family in the first week after referral. Both the mother and husband were seen thereafter once weekly and the patient twice weekly. In these initial sessions, a decision was made to discontinue all medication since the patient reported that she was terrified of taking them and did so solely because of her family's urging. It is of interest to note that the patient had developed a phobia about the taking of all drugs. Antihistamines, antibiotics, tranquilizers, and even aspirin precipitated the same reaction of panic and feelings of depersonalization.

The patient's mother reported that she felt that it was not right for her to assume all of the patient's duties. She stated that she was anxious to return to her home but felt that she could not do so under the present circumstances. She was reassured that a goal in treatment was to enable the patient to re-assume the care of her household. She was urged to try to involve the patient whenever possible in her usual duties. The patient's husband was encouraged to return to his professional work. He was extremely anxious, and realistically so, about the increasing loss of time from his duties. In bi-weekly family group sessions, the eventual prospect of the mother's leaving and the patient's assumption of her usual role was discussed. At first, the patient was unable to entertain such a possibility but gradually came to feel that it was desirable and something to work toward. Within 3 months of the



initial contact, the patient's mother was back at home in the midwest and the patient had resumed most of her household duties. Her husband, at this time, was satisfying his professional obligations and was able to contribute in a more constructive way in his home.

### **Patient's Past History**

The patient was born in a small midwestern town. Her mother recalled that she was a cheerful, sociable child. The patient's father died when she was four years of age and an older brother became the male mainstay of the family. The patient stated that she had never "gotten over" the death of her father and had been unable to attend funerals or to think about death throughout her entire life.

She remembered her school years as happy and productive. A good student, she had many friends of both sexes. She met her husband before her college graduation and was married within the next year. She had attended a college near her home and had almost daily contact with her mother and older siblings throughout her college career. Shortly after marriage, her husband's business took him to the east coast. After they moved, she found herself "homesick" and completely unprepared to adjust to the new situation. She viewed the people in her social stratum as wealthier, more articulate, and more sophisticated than she. Subsequent information indicated that this view was most unrealistic. She avoided ordinary kinds of social contact and found herself systematically isolating herself and her husband as a couple.

She related that she never really liked or felt comfortable with her new home. She became overly concerned with her routine household duties. Her behavior toward her husband became demanding and argumentative. The husband related that he found her behavior very trying, causing him to have periods of moroseness. However, neither could admit that anything was wrong. They maintained that their marriage was untroubled, each privately hoping that their relationship would improve. Sexual relations became relatively infrequent. One of them would be "too tired."

Although she used a diaphragm and consciously did not want another pregnancy, she "found herself" pregnant with her fourth child. In retrospect, it seems that the pregnancy was an attempt by the couple to reassure each other about their marriage. Privately, both had frequently fantasied about divorce but neither had been able to admit the existence of such thoughts either intrapsychically or to each other. When the patient discovered that she was pregnant for the fourth time, she began to be troubled by the thought that she really did not want another child. On the few occasions when she

was able to focus on this thought, she had a deep feeling of moral repulsion. In her view, having such thoughts was sinful, setting her apart and making her different from other women. She began to overeat in the evenings, feeling that she could not get through another day of feeling tired yet having to meet the demands of her family. It is important to point out that the patient projected this as an unending process. No relief was envisioned in the future. To maintain certain fictions about herself and her marriage, however, this whole area of feelings could not be expressed or shared with anyone.

Following the birth of the fourth child, the patient felt a transient sense of relief. However, she slowly began to realize that the former cycle of demands was now returning to an increased degree. With no relief in sight, feelings of rage developed in the patient. She wished to strike back at what she experienced as a confining and punitive environment. In this general setting, her symptoms appeared.

### **Course In Psychiatric Treatment**

The psychiatric treatment process can only be sketched briefly. The patient has been seen in therapy for 2½ years to date. For the first few months, treatment was on a bi-weekly basis; later, the patient was seen once weekly and most recently she has been seen bimonthly. During the first year of treatment, the patient asked the therapist in many different ways if he were really interested in her and if he would continue with her until she was well, reflecting her expressed statement that she was completely dependent upon the therapist. She brought in many questions about her behavior, asking what she should do or how she should understand certain events which occurred. It seems useful to conceptualize her behavior during this initial phase as testing the limits, stability, and genuineness of the relationship with her therapist.

During this time, any attempt on the part of the therapist to discuss termination was met with a phobic, extremely anxious response on the part of the patient. She stated that she was unable to tolerate any thought of terminating but work was performed on the question of termination in each session. During this time, the patient insisted on asking questions about depression, schizophrenia, and cancer. These attempts were interpreted as her means of externalizing problems which she could not deal with in any realistic way. As time passed, she slowly improved. Her phobic difficulties in her home and her fear of going out of the house to shop or visit were among the first to disappear. She gradually became able to tolerate visitors and it is of interest that she was able to resume rapidly her relationship with her 3 older children so that they

were spared from seeing her more severe symptomatology. The patient experienced more difficulty in taking care of her infant but by the end of the first year of treatment, she was caring for him and was able to celebrate his birthday without incident.

During the second year of treatment, the psychotherapeutic focus shifted quite dramatically. The patient's questions no longer centered on depression and schizophrenia and she began to speak about the problems in her marriage, her obesity, her disappointment in herself and about some of her less mature characteristics. By the time she had been in treatment for 18 months she was, in essence, a different case. All of the phobic and anxious symptoms had disappeared with the exception of chronic fatigue and occasional panic. The patient's husband was seen occasionally at this time and whenever there seemed to be some issue between them that justified formal scrutiny. One of the chief issues dealt with was her ability to permit him to go on professional trips. She had fantasies that he would die, not return, or that he would abandon her and she would then have to be hospitalized. Significant therapeutic advances were made around the issue of his leaving and questions of termination with the therapist were woven with these incidents.

Most recently, the patient has been thinking about termination but has stated that she would feel more comfortable having occasional visits. A decision has been made not to terminate formally with this patient and she is being seen twice a month. She uses her treatment hours to review her illness and seems, at present, to be struggling to organize her recent life experiences. With the exception of mild fatigue and overeating, she is presently symptom free. She is socializing in a way which was not possible for her even prior to her illness and has begun to deal realistically with the problem of how to gain gratification for herself. She has become active in community affairs in what seems a sensible and rewarding way.

### Discussion

There are probably multiple etiologies in postpartum emotional disturbances. Current reviews of the problem<sup>1-3</sup> point out that puerperal infections, formerly a common cause of post-partum psychoses, no longer occur with appreciable frequency. While some maintain<sup>2</sup> that altered somatic states secondary to the stress surrounding delivery are etiologic, others tend to adapt a stress summation theory. According to this theory, a patient who develops a post-partum depression or psychosis is, at the time of delivery, undergoing multiple stresses. Marital difficulty, inability to adjust to the demands of parenthood, chronic anxiety secondary to unre-

solved dependency upon the mother, the anticipation of an increased work load following the birth of the child, and a growing conviction that there is no release from such a set of difficulties, are examples of pre-existing stresses which, combined with the stress of delivery and the subsequent realization that a poor situation is now worse, precipitate a major psychiatric reaction. Somatic factors are not excluded from this formulation, but are viewed as interacting with all other variables.

In the case under discussion, this theory offers a more comprehensive and psychologically coherent etiologic formulation than a simple theory of altered somatic states. It has the further advantage of directing the physician's attention to emotional and familial variables. We have seen that many physicians accepted the patient's explanations of her difficulties without assessing her total situation. Antidepressants were prescribed probably on the implicit assumption that the patient was suffering from biochemical and/or physiologic alterations. The patient's and the family's defensive operations were thereby given medical sanction.

It should be pointed out that although the concept of stress summation is useful in describing etiology, other concepts are necessary for an understanding of the progression of this patient's disease. Her illness occurred in a social and medical context; certain kinds of interaction between the patient, her family, and the medical community were necessary for the disease to progress as far as it did. The mutual reinforcement on the issue of etiology has been alluded to above. Other interactions serving to foster the progression of her illness revolved around the structuring of her behavior consequent to her perception of the roles of the various physicians she visited. Her presentation of "general practice" complaints to her family physician, "obstetric" complaints to the obstetrician and her presentation to the psychiatrist as being more psychologically disintegrated than she really was, illustrate how well attuned this patient was to the roles of various specialists. An appreciation of the influence of such role perceptions in her behavior allowed for an accurate estimation of the severity of her illness. Thus, a psychiatric hospitalization was avoided and a treatment program geared to her true needs could be instituted. At present we have no appropriate term to describe this element in the behavior of patients. "Role specific" or "situational specific" would seem to have to serve to describe elements in the behavior of patients which result from their perceptions of the particular interests of the physician they are visiting. An appreciation of the existence and meaning of such behavior might have led to earlier



recognition and saved this patient and her family a great deal of suffering.

The patient's phobia about the taking of all forms of medication deserves a closing comment. In the course of treatment the patient's ruminations about suicide and infanticide emerged. A complex of feelings around such fantasies seemed to be involved in the drug phobia. First, the patient feared that she now had a means for doing away with herself and/or her infant. Secondly, she seemed to fear that the drugs would cause her to lose her very tenuous control over these impulses. Given these considerations, it seems clear that an aggressively pursued chemotherapeutic regimen would probably have delayed or perhaps obstructed the patient's recovery.

In summary, this case suggests that post-partum emotional reactions deserve the same close attention given any other psychological disturbance. A multi-

factorial etiology is probable and theories attributing the syndrome to "exhaustion" or altered somatic states can lead to serious errors in diagnosis. Close monitoring of the psychological response to psychoactive medication is always necessary. Finally, a physician should be aware of the influence of his particular medical role on both his own and his patient's behavior.

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**DECEPTION OF THE ELDERLY**

U. S. Senator Harrison A. Williams (D-N.J.), chairman of a new Senate Subcommittee on Consumer Interests of the Elderly, states: "Americans past 65 years of age now have a total buying power of nearly 40 billion dollars a year . . . (and) we on the Subcommittee will maintain a lively interest in outright frauds and deceptions that exploit the elderly."

Approved for publication by the Council, the CSMS Committee on Aging has made a recommendation that "physician members of the Society be encouraged to report to the Committee instances in which it is suspected or known that old people are being taken advantage of or are not getting value received from the providers of (medical) goods or services."

Reports of such instances may be addressed to: Kurt Pelz, M.D., Chairman, CSMS Committee on Aging, 330 Harrison Road, Wallingford, Connecticut, 06492.

# Psychiatry In The General Hospital

Stephen Fleck, M.D.

## I. Introduction

■ Historically psychiatry is both the oldest and the youngest clinical discipline. Much treatment through the ages depended entirely on the psychological elements in the physician's prescription, whether so recognized by him or not. As scientific bases for therapeutics developed, and the physician became increasingly certain of what could work and what didn't he also became more modest if not even disdainful of his impact as a person on his patients.<sup>12</sup> Benjamin Rush 175 years ago did not hesitate to state: ". . . I have frequently prescribed remedies of doubtful efficacy . . . , but never till I had worked up my patients into a confidence, bordering upon certainty of their probable good effects."<sup>17</sup> The modern physician feels almost obliged to ignore, as if he thereby could eliminate such personal impact on the therapeutic process, especially when evaluating drugs or other measures. "Scientific" has become equated with "impersonal" or "minimally personal" as if the definition of scientific depended only on the reproducibility of a process or effect, irrespective of interpersonal variables.

Only since Freud has modern psychology brought scientific scrutiny to the processes between people and their impact on each other. But by then psychiatry for many reasons had left or had been excluded from the main stream of medicine, especially in this country. Fifty years ago there were few medical schools with any psychiatric faculty; community or municipal hospitals, including a few affiliated with medical schools, often had holding units for psychiatric patients preparatory to their proper transfer to distant mental hospitals, but only The Johns Hopkins and Pennsylvania Medical Schools had their own pavilions for the study and treatment of mental patients at that time. Then, stimulated by psychiatric experience in World War I especially by Southard,<sup>21</sup> several medical schools established or affiliated themselves with psychopathic hospitals usually small replicas of the larger mental hospitals, which because they served limited areas and populations and included out-patient services, became the forerunners of today's Community Mental Health Center, as prophesied by the dean of American psychiatry, Adolf Meyer.<sup>15</sup>

Psychiatry did not return to the university hospital proper until the mid-thirties, when the Massa-

chusetts General Hospital opened a ward under Stanley Cobb. Now there are over 1,000 such units in the United States, but only seven in Connecticut. These units vary greatly in size and in type of service and serve very different populations. We shall describe here principally the operation at the Yale-New Haven Hospital (750 beds) but also point out general considerations whether operative at the Yale-New Haven Hospital at present or not. Moreover, there are differences between university-affiliated services with their threefold mission of service, teaching and research, and units in hospitals not so affiliated.

The present-day psychiatrist has fallen heir to those functions of the traditional family physician which patients value most: the personal interest in, and long-range knowledge of, the patient and his family. This informal and usually unconceptualized knowledge is indispensable in the evaluation of symptoms and the understanding of changes in the disease course, and thus an essential ingredient of therapeutic effectiveness, aside from furnishing possible etiological clues. The psychiatrist as a student of human behavior is the relative expert in this psychosocial sector of medical care, because other specialists have lost or are being deprived of the opportunity to know patients and their families well over time due to the discontinuity of medical care and the subspecialization according to organ systems. Medical services have become fragmented at the expense of continued familiarity between patient and physician in the community as well as in the hospital. Gaps in care have arisen because often the family physician cannot care for his patient inside the hospital, and because the hospital-based specialist often cannot follow him out side. But even within the hospital the complexity of disease problems often requires the involvement of several specialists, so that not only the patient but sometimes the staff become uncertain which specialist is THE doctor for a particular patient. The psychiatrist enters this interregnum in the general hospital as the one specialist who focuses on the patient as a biopsychosocial unit, competent to discern and assess rather quickly the patient's

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emotional state and the biological, psychological and social variables relevant to the clinical situation. He does so by focusing on the patient's longitudinal experience, on his history and personal development. This can be at least a substitute for long-term acquaintanceship with the patient and his significant social surrounding, because the psychiatrist understands the psychological and social referents and the emotional implications of historical and behavioural data, and with the help of this understanding he can form rather quickly a close relationship with the patient—as if they had known each other a long time. Thus although a specialist, the psychiatrist focuses on “a particular part” of the patient only as the patient's own story, not necessarily his chief complaint, may induce the skilled listener to narrow his interests towards either a symptom cluster, a behaviour pattern, or a particular life event. Furthermore, the present-day hospital psychiatrist has acquired a relative expertise in patient care and care continuity in the community, because psychiatrists have had to recognize and cope therapeutically and administratively with these particular problems in mental institutions in the last two decades.<sup>4, 10, 13, 14, 20</sup>

**II. Types Of Service**

While the NIMH has stated that no general hospital deserves this designation unless it provides beds for psychiatric patients, this does not necessarily mean the establishment of a separate ward or service; nor does it follow that a hospital should go ahead with providing beds before examining total community needs and taking into account already existing psychiatric facilities in that community. From the manpower standpoint, psychiatry can no more afford competitive duplication of services than can any other medical branch or specialty at this time. The establishment of a psychiatric unit in the general hospital must be reconciled with the givens of psychiatric practice in a community to ensure its proper place in a network of mental health services, most of which need not be under the hospital's control. Existing services, and others planned for extra-hospital location, determine the range and policies of services which the hospital must provide under its aegis and within its walls in a particular community. A full-range general hospital psychiatric program should function like a small scale community Mental Health Center.<sup>12, 20, 22</sup>

**A. IN-PATIENT SERVICE**

Full-time in-patient services will be the type most likely needed in the community, and like other in-patient services represents the core of the hospital psychiatric department. But the number of beds need not limit the number of patients, as day and

night patients can be accommodated in the same facility, and programs for both can be integrated with those for full-time patients.<sup>9, 10</sup>

Patients in need of around-the-clock care demand around-the-clock professional attention. This pertains to competent nursing and ancillary personnel, and a full-time psychiatric staff, at least on the resident level, is essential. A high staff-patient ratio is particularly important if complex diagnostic tasks are to be accomplished expeditiously. A complete evaluative study of a psychiatric patient includes routine medical, psychiatric and neurologic examinations and a thorough investigation of the patient's family as individuals and as a group, and possibly of other psycho-socially significant persons. Such an “admission” study, which covers the biological, psychological and social parameters of personal functioning, may take up to a week, and sometimes longer if significantly related persons live at a distance, and it requires team work. The observations of social workers, nurses and aides of the patient and his visitors and of all their interactions with the ward population are equally as important as the psychiatrist's mental status record, or the EEG, or drug levels in body fluids.

Because team work is essential, and more important than which particular professional deals with a particular aspect of the patient's problems whether for evaluative or therapeutic purposes, it is necessary to spell out the requisites of team work. A team (or in community practice a group) exists by virtue of its communicative qualities. It is not just a collection of people working in the same place even if they work towards the same goal. The psychiatric team consists of different specialists, professionals and non-professionals, but what they must bring to team work is not only their particular expertise, but a collegial attitude towards all team members, a readiness for role diffusion and a capacity to provide and suffer critical scrutiny of the interactive processes on the ward, including the scrutiny of one's own behavior by oneself and others. In this way the “personal” impact on the patient is under continuous observation as is awareness of the milieu climate. The free and self-observant communication among staff also subserves in essential ways teaching functions and clinical research. To create such a therapeutic environment requires a number of different group meetings with and without patients, with and without families, all of which has been described in detail elsewhere.<sup>7, 9, 11, 20</sup>

This model of “shared doctor-patient relationship” applies also to non-psychiatric practice inside and outside hospitals, because only a team or group of specialists as defined above can now provide the best up-to-date medical care to patients with complex problems, combining care continuity with in-

tegrated technical and intra- and interpersonal expertise. Thus, even if the psychiatric service does not extend its activities into other hospital areas, it still can serve as a model for the care of non-psychiatric hospital patients. Separate psychiatric services in the general hospital with a full-range professional team are therefore preferable to caring for psychiatric patients in any available bed in the hospital. Although feasible, this latter arrangement should be limited to small hospitals with so few psychiatric patients as to render a full-time psychiatric team highly uneconomical.

The psychiatrist in the general hospital should, of course, be a competent psychotherapist, but he must not be committed to a single treatment modality. Parallel to the broad-range evaluation, treatment decisions should also be based on a careful evaluation by the team of the relevant biopsychosocial forces and how these might be affected favorably through a single approach or a combination of therapeutic measures in all three spheres. Evaluation of the patient's family or other emotionally significant surroundings is particularly important, because often it is possible through family meetings and therapy to effect a change in the equilibrium of this group enabling the patient to recover from an acute crisis, as well as ensuring the improved functioning of all concerned through stabilization of such a new equilibrium. This family-oriented diagnostic, therapeutic and preventive focus is also applicable to other hospital services.<sup>5, 7, 10, 13</sup>

By and large there will rarely be enough time and manpower to embark upon intensive individual psychotherapy with a patient, but the experience can well be utilized to prepare the patient for such treatment and to arrange it, possibly to begin before the patient's discharge. Electroshock treatment should be administered when indicated on an in-patient service. Drug regimen also should be established in the hospital to determine safe and therapeutically effective levels for each patient and should further be controlled carefully during the period of his rehabilitation into community life.

#### **B. CONSULTATION SERVICES**

Ideally a psychiatric service in the general hospital does not limit its activities to the care of psychiatric patients per se. We have referred already to the complexity of modern in-patient care and the frequent fragmentation of the doctor-patient relationships because of the many different experts who must be involved with the same patient. The antidote to this fragmentation is the "shared doctor-patient relationships" through a team as defined above (p. 2). So far non-psychiatric specialists have formed such teams only around very special treatment situations such as

operating rooms, dialysis procedures, the prematurity unit, the intensive care unit, etc. Intensive care units and recovery rooms, however, carry special psychogenic elements in the form of monotony of surroundings, anxiety arousing gadgetry, and the patient's physical and mental exhaustion abetted by anesthetics or other drugs, or metabolic dislocations, or both. Here psychiatric expertise is called for to scrutinize such special treatment units and recommend measures designed to prevent psychotic disorganization.\*

Patients also still die in hospitals, and the psychiatrist is often needed in the management of terminal illnesses to help define the patient's behavior and attitudes in this situation; to guide and assist him and his family in the difficult task of maintaining contact without overwhelming stress; and to support the staff and prevent the patient's isolation from hospital personnel, sometimes sorely burdened by almost constant confrontation with death and dying. The medical profession's commitment to saving and preserving life can bring about two interrelated conditions which interfere with the patient's emotional and interpersonal needs, and often deprive him of the opportunity to die in dignity and peace. Death is often experienced by us as failure, and the decision to treat a hopeless condition vigorously is often rationalized as "not playing God," with the result that treatment measures are continued at the expense of the patient's comfort despite evidence of their ineffectuality.<sup>19</sup> In this way patients and their families are often prevented by a guilt-motivated professional staff from meeting these grievous situations spontaneously and sharing their feelings according to their style, unencumbered by a covert conspiracy not to talk about it, and face the obvious together. This can lead to serious emotional disorder and suffering for the patient and for family members, besides depriving the patient of the opportunity of dying in a dignified manner as a whole person emotionally and psychologically, even if he cannot be whole in a physical sense. The psychiatrist and his team (and some spiritual advisors) can and must help their colleagues who are more closely involved than he with the every-day problems of maintaining and effecting a realistic program for the patient as a person in addition to fighting malignant cells or dialyzing body fluids, and the psychiatrist should therefore be a member of cancer treatment teams and others dealing with terminal illnesses.<sup>1, 19</sup>

In a teaching hospital psychiatrists should also be regular participants on all in- and out-patient services and on teaching rounds, both to identify psychiatric problems in patients with or without other illnesses, and to help non-psychiatric physicians

\* See F. P. McKegney: The Intensive Care Unit. This issue.



and other staff to deal therapeutically with both these types of patients. Besides helping the patient directly, the psychiatric team demonstrates team work and ensures that all staff members concerned with a particular patient have the opportunity for and educational benefit of such consultations. Another function of the consultation practice is to prevent referral of acutely psychotic patients to the psychiatric service when the psychosis is presumably of short duration, such as a drug-induced confusional state.<sup>3, 4, 18</sup> This is particularly important if such patients also need complicated specialistic surgical or medical care for which the psychiatric ward may be poorly equipped or staffed. In the 750-bed Yale-New Haven Hospital the consulting psychiatrists see currently on non-psychiatric in-patient services about 600 patients a year, of whom less than 5 per cent are transferred to the 24-bed psychiatric in-patient unit.

### C. OUT-PATIENT SERVICES

Besides beds and other space for full- and part-time in-patients, the hospital should provide ambulatory services and assume collaborative responsibility for the establishment of a network of community-based facilities for the mentally ill. Agencies are needed for the after-care and rehabilitation of discharged hospital patients, or at least for preventing their becoming disabled again and requiring rehospitalization. Such facilities include halfway houses, family agencies, rehabilitation services and sheltered workshops, as well as psychiatric consultative services to these and other institutions such as schools, well-baby clinics, visiting nurses, etc. In brief, the psychiatric out-patient service should function and define its aims in accordance with its appropriate place and position in the network of community services and the limitations imposed by the hospital's staff and other resources. However, if the hospital provides ambulatory services for non-psychiatric patients, psychiatric consultation should be made available to such clinics on a routine basis. Here also team consultation should be used when indicated, including the employment of a psychiatric visiting nurse for home and family care.

If the hospital runs an in-patient service, follow-up care for these patients should be provided although not necessarily requiring a separate out-patient facility. Again it depends whether most if not all such former in-patients return for continued care to community resources apart from the hospital, or whether there are no such resources, in which case the hospital should provide them either through a separate clinic or through a staffing pattern on the in-patient service which permits the continuation of treatment by the in-patient team after the patient's discharge. Various combinations

of these alternatives may be best suited to particular local circumstances. For teaching purposes some continuity of care across the administrative barrier, which discharge from an in-patient unit often constitutes, is essential, and no doubt desirable for many patients.<sup>11, 20</sup>

Services for out-patients referred from the community or from other hospital services should also be provided on an interdisciplinary team basis, including at least psychiatrists and social workers, but preferably also nurses and psychologists. Treatment should cover the same modality range as on the in-patient service, except for electric shock treatment. The composition of therapy groups in out-patient work should be more determined by diagnostic, personality type, and social class considerations than is possible on an in-patient service. If children and adolescents are served, special treatment programs for these two groups may be in order and this may also pertain to very old patients. Again, this obviously depends on the availability of equivalent psychiatric or ancillary resources in the community, such as special clinics for alcoholics and other addicts, or programs for marital counselling and family therapy.

Usually clinics will be confronted with many more demands and expectations for service both as to type and numbers than can be fulfilled adequately. While it is the hospital's mission to supply services which it can provide better than other agencies, it is also its responsibility to define the limitations of what it can accomplish, and what it proposes not to do in a positive way, by pointing out service needs to the community and cooperating with it in providing other extra-hospital-based resources. For instance the hospital can employ its own visiting nurse for home treatments and family evaluation, or it can work with an independent visiting nurse agency to accomplish this.

### D. CRISIS SERVICES

Although of the 40,000 emergency visits to the Yale-New Haven Hospital only about 3 per cent are for explicitly stated psychiatric reasons, it is estimated that usually about 10-15 per cent of patients coming to a hospital emergency room are primarily psychiatric.<sup>6, 8</sup> This proportion is apt to be higher when the hospital is known to provide psychiatric services. Moreover it has become increasingly apparent in the past decade that many patients use the emergency room as the only available around-the-clock medical resource whether their problem is emergent or not.<sup>22</sup> This is so particularly in teaching hospitals with ample house staffs, but around-the-clock coverage of emergency services is mandatory whether through house staff or regular staff members. The psychiatric problems in the emergency room run the full range of diag-

nostic and behavioral entities, but without exception there will be also psychosocial ones.<sup>8</sup> Often close cooperation with the non-psychiatric physicians is essential, for instance, in cases of suicidal trauma or poisoning, alcoholism, or in the differential diagnosis of unconscious states, etc. Here again the educational impact of the demonstration of up-to-date psychiatric approaches is important. The concepts of crisis as formulated by Lindeman and Caplan, and therapeutic crisis intervention following evaluation of the psychosocial disequilibrium, lead to multifaceted measures to improve this imbalance.<sup>5, 14, 16</sup> These are not only essential therapeutic steps for the patient and his immediate surrounding, but important paradigms of family-focused medical practice and team work.

Psychiatric crisis care cannot be carried out in the usual emergency examining and treatment room. There must be available quiet interview areas including the opportunity to conduct hypnosis or sodium amytal interviews, and room for interviewing significant relatives apart from the patient and together with him or to meet with a group, most likely the family. Beds to hold patients overnight or even longer should be provided to gain time for staff to contact significant relatives or others, if necessary through home visits. A certain percentage of patients can of course be transferred promptly to an appropriate in-patient facility, but it must be kept in mind that this number is probably reducible in proportion to the extent and adequacy of crisis management. At this time we have not plumbed the extent of therapeutic and preventive effectiveness of comprehensive crisis management, so that we cannot now know the irreducible minimum number of patients who cannot be helped in this way.\* Equally unknown at this time is the effectiveness of the various types of suicide prevention services established in recent years in many communities, because of the short time since most of these services have been instituted.<sup>6, 7, 16</sup>

### III. Administrative Aspects

Another view of general hospital psychiatry can be gained by examining the roles of the psychiatrist in such an operation. While the total range of such roles will be briefly outlined in this section, this is not to imply that one psychiatrist would or could fulfill all these functions, but to emphasize three points. (1) The psychiatrist must always orient himself as to which role he is playing, or is asked to assume, in a particular activity; (2) he must decide which roles and areas of professional

activity he delegates and assigns to others, or leaves undone and uncovered; and (3) he must establish priorities for the development of services, and also for teaching and research, through participation and collaboration with his non-psychiatrist colleagues and with professional and non-professional authorities. The distinction between participation and collaboration in this context is that as a participant he negotiates about and integrates the psychiatric area of responsibilities with non-psychiatric colleagues who have equivalent responsibilities for other services in the hospital or for the educational programs. Collaboration with the same and other individuals denotes the joint efforts for a superordinate mission, for instance hospital-community relationships, or the establishment of community resources which are of concern to the hospital, but not its direct responsibility. The psychiatrist will also become involved in, or at least will be approached about personnel problems. In such functions he must take care to delimit his role either to that of consultant to the administrative staff or of therapist, although he may wisely defer this decision as to role assumption until after he has evaluated the problem thoroughly, including interviewing the individual or individuals involved.

In other roles the psychiatrist participates in establishing hospital policies, in selecting key personnel for services and faculty of a teaching hospital, and he also represents the hospital in the community as a specialist, or as a staff member. The psychiatrist further participates in decisions about service needs in the hospital, space allocations, budgetary matters and all the many facets of providing and facilitating patient care and treatments.

Next he is chief of the psychiatric service or services, as well as consultant to other services. He must provide supervision and guidance to subordinates, especially residents who carry out most of the therapeutic work with patients, and collaborative supervision to the other mental health professionals. Research must be facilitated and supported. His role as therapist and psychiatric team member has already been discussed. The Yale-New Haven Hospital psychiatric services comprise currently ten full-time psychiatrists, two psychologists, seventeen psychiatric residents, twenty nurses, practical nurses or aides, and over twenty psychiatrists who serve as part-time teachers, supervisors and consultants to non-psychiatric services.

It was asserted in section II.A that there should be full-time psychiatric staff on the in-patient service. This does not preclude treatment continuity with a psychiatrist who has been caring for the patient before hospital admission. But the control and decision as to the role of the "outside thera-

\* The Connecticut Mental Health Center to be opened this year in New Haven is preparing to undertake such a study under Doctors Claudewell Thomas and Marc D. Schwartz.



pist" during and after hospitalization should be in the hands of the hospital psychiatrist, and based on the team's around-the-clock evaluation of the patient and his problems. Of course the therapeutic relationship should not be disrupted automatically by hospitalization, but a patient who after prolonged office treatment needs hospital care, no matter how temporarily, should be studied thoroughly, and this includes consideration of the role and effectiveness of the therapeutic relationship and work prior to hospitalization.

Summary

The guiding principles of psychiatric services in the general hospital have been presented. These concern essentially two sectors: (1) Services to psychiatric in- and out-patients which should be integrated with extra-hospital mental health services and function like present-day community mental health centers; and (2) educational influences on non-psychiatric staff with regard to patient care and the organization of care. Modern psychiatric care methods, especially the team principle, the focus on the family as a unit and other psychosocial issues, have applicability to non-psychiatric services, and the roles of the hospital psychiatrist in carrying out these functions have been sketched.

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# The Connecticut Mental Health Center

## A Joint Venture Of State And University In Community Psychiatry

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and John F. O'Connor, M.P.H.**

### I. Introduction

■ Psychiatry is presently in the midst of rapid changes and some of the most exciting and important developments and concepts are in community psychiatry. American psychiatry has moved increasingly toward treatment programs aimed at maintaining the patient in his own home and local community. At the same time, research and teaching have become more and more concerned with these developments.

Since World War II, psychiatry has seen the favorable results of milieu therapy and of group therapy. New drugs have been developed that relieve distressing symptoms. Effective intervention during crisis can be undertaken and there is an enhanced interest in after-care and social and vocational rehabilitation. Advances in psychiatric knowledge and treatment have been paralleled by significant changes in community attitudes toward the mentally ill. These changes in attitude are reflected in greater tolerance toward mentally ill neighbors and relatives and in the willingness of local, state and federal legislatures to appropriate funds to improve existing mental health programs and initiate new ones.

The development of mental health centers in many communities results from the convergence of these trends. The Connecticut Mental Health Center, its construction recently completed, in New Haven, is a collaborative venture of Yale University and the State of Connecticut. It is illustrative of the University-affiliated state facility that has developed in a number of places, e.g., the Massachusetts Mental Health Center and the New York State Psychiatric Institute.

The historic roots of community psychiatry can be traced back to Clifford Beers who founded a world wide citizens' movement, the Committee for Mental Hygiene, in New Haven in 1908<sup>1</sup> and to the late Adolf Meyer, whose 100th birthday American psychiatrists are now celebrating, who stressed the importance of preventive work through extramural efforts outside of the hospital.<sup>2</sup> More recent milestones were the development of the concept of the therapeutic community by Maxwell Jones,<sup>3</sup> the establishment of the open hospital and vocational

rehabilitation by such British hospital superintendents as Rees, Jones, Duncan, MacMillan, and Freudenberg, and Americans like Hunt, Barton, and Greenblatt. Querido in Amsterdam found teams of mental workers in the community more important than hospital beds.<sup>4</sup> Lindemann<sup>5</sup> and Caplan<sup>6</sup> provided important concepts for community psychiatry; e.g., crisis intervention and continuity of care.

The immediate origins of the community psychiatry movement may be found in the report of the Joint Commission on Mental Illness and Health authorized by Congress in 1955. This commission organized a five year survey in order to analyze and evaluate the needs and the resources for care of the mentally ill in the United State and published its report as *Action for Mental Health* in 1961.<sup>7</sup> In February, 1963, President Kennedy delivered his now famous message to Congress on mental health and mental retardation. The substance of his message was subsequently embodied in Public Law 88-164, the "Mental Retardation Facilities and Community Mental Health Centers Construction Act of 1963" which authorized federal matching funds for use by the states in constructing community mental health centers. More recent legislation has expanded this program to include support for staffing by a matching formula with the federal percentage declining over four years. As a result, a considerable number of programs are now under way throughout the country; there will ultimately be a network of local mental health centers and a phase of rapid expansion of psychiatry and of mental health facilities and programs can be anticipated.

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Planning activities in the field of mental illness and health were undertaken, with the help of federal funds, in every state in the union in 1963-65. Connecticut's plan for comprehensive mental health services, derived from the effort of thousands of citizens in all regions of the State, was presented in November, 1965 to Connecticut's First Mental Health Congress.<sup>8</sup>

**II. The Establishment Of The Connecticut Mental Health Center**

The decision to establish a mental health center in New Haven preceded by several years the current nationwide emphasis upon the organization of community mental health centers. The Connecticut Mental Health Center was conceived in the 1950's as a university-affiliated State facility that would be simultaneously engaged in offering exemplary care for patients, in the training of personnel and in the conduct of research.

In 1959, the General Assembly authorized the establishment of a mental health center in New Haven; Special Act 406 of the legislature appropriated funds for preliminary survey and planning. In 1963, Public Act 579 was adopted by the General Assembly, establishing the Connecticut Mental Health Center as a facility of the Department of Mental Health to be operated in collaboration with Yale University through mutual agreement.

The five-million dollar building that will house the Connecticut Mental Health Center was ready for occupancy in early summer 1966. Immediately adjacent to the Yale-New Haven Medical Center, the Connecticut Mental Health Center is located on Park Street, near the York Street Exit of the Oak Street Connector.

The building has 64,555 net square feet of space and includes areas for a 30-patient day treatment center, two 22-bed inpatient treatment units, a large outpatient program, a small unit for brief hospitalization (72-hour) of emergency cases, and a 22-bed residential study unit with adjoining research laboratories. There is also a 140-seat auditorium, classroom, a library and a cafeteria.

The building design has two wings; the ground floor contains administrative and faculty offices, an admissions suite, a communications center, and the 7-bed unit of the Emergency Treatment Service. On the second floor are the outpatient facilities, the Day Hospital and the main cafeteria. The third (top) floor of one wing is devoted to research laboratories. The inpatient units occupy the third, fourth, and fifth floors of the other wing. The stack between the two wings contains elevators and service facilities.

The construction costs for the Connecticut Mental Health Center have come from a number of sources.

In 1961, the State legislature authorized a bond appropriation for construction funds. Other funds came from the National Institutes of Health and Yale University.

**III. General Aims And Purposes**

The Connecticut Mental Health Center will have five major purposes:

- (1) To provide exemplary diagnostic services, treatment, aftercare and rehabilitation to patients suffering from a wide range of psychiatric conditions.
- (2) To initiate and conduct a broad program of research, of clinical investigations of mental illness, of intensive biological studies, as well as studies of the social and institutional contexts of psychiatric illness and treatment.
- (3) To undertake the training of mental health personnel particularly psychiatric residents, clinical psychologists, social workers, psychiatric nurses and medical students, as well as a program for the training of non-professional workers. The Center will participate in programs for psychiatric training and consultation for physicians in the region.
- (4) To develop models of patient care and of training that can be applied elsewhere in the State and nation. By studying the operation of the day hospital, for example, a useful model can be developed that others can apply or can adapt to their needs and resources.
- (5) To participate in the development of comprehensive community mental health services for the greater New Haven area. The specific clinical programs of the Connecticut Mental Health Center will be a major part of an overall program for the greater New Haven region. The Center staff expect to work closely with the South Central Connecticut Regional Mental Health Planning Council, the other hospitals of the State Department of Mental Health, and community agencies. The staff look forward to the establishment of close relations with local physicians, clergymen and other professional people who are called upon to deal with problems of mental illness and mental health.

In developing its programs, the Connecticut Mental Health Center thus has a dual aspect; it will be both a major community mental health facility for the greater New Haven area, and a University center for training and research whose responsibilities are world-wide.

The geographic area within which we expect to provide the bulk of our clinical services extends from Milford on the west to Madison on the east and coincides with the South Central Connecticut

Mental Health Planning Region.\* Included within it are the communities that participate in the Greater New Haven Community Council and United Fund and are served at present by the Battell Unit of the Connecticut Valley Hospital.

The total population of the area is from 300,000-400,000 persons. The Connecticut Mental Health Center will not by itself be able to serve all the mental health needs of the region. However, it is the conviction of the staff that by working closely with the Connecticut Valley Hospital and its Battell Unit and with other state and community agencies, a comprehensive program will evolve.

#### **The Connecticut Mental Health Center, Yale University, and the State**

The Center is the *Connecticut* Mental Health Center to the extent that its training and research activities will have State-wide impact. Experience gained at the Center will contribute to the development of mental health programs in Connecticut. Many of the personnel trained at the Center can be expected to remain in the region. Previous experience indicates that professional persons trained here decide in large number to practice in Connecticut. Moreover, the experience gained at the Connecticut Mental Health Center will, it is hoped, be applicable to other mental health centers now being planned for Connecticut. As a University-based mental health center, emphasizing research and training, there are excellent opportunities to develop models of clinical care and of community-University relations. One example of the latter is the attempt to develop a program in Administrative Psychiatry by members of the Connecticut State Department of Mental Health and the Departments of Public Health and Psychiatry at Yale University.

One of the major innovations in the creation of the Connecticut Mental Health Center was the provision for a contractual arrangement whereby senior professional personnel at the Connecticut Mental Health Center are employed as Yale University faculty with a proportion of their salary being provided to Yale by the State of Connecticut. The professional staff will be engaged in patient care, in teaching and will participate in research programs.

#### **IV. Specific Programs Of Clinical Service**

Within the scope of its general aims, the Connecticut Mental Health Center will offer nine programs of clinical service:

\* Bethany, Branford, East Haven, Guilford, Hamden, Madison, Milford, New Haven, North Branford, North Haven, Orange, West Haven, Woodbridge.

#### **(1) DIAGNOSTIC ASSESSMENT**

Careful assessment and diagnosis are central to medical care and will be emphasized at the Connecticut Mental Health Center. For each patient, a tentative psychiatric diagnosis and psychosocial formulation will be offered as well as a preliminary statement of therapeutic goals and recommended treatments. These formulations can then be reviewed in the light of the patient's progress.

#### **(2) EMERGENCY TREATMENT**

The Connecticut Mental Health Center will add to the already existing emergency facilities in greater New Haven. A significant proportion of patients will, of course, require emergency care.<sup>9</sup> This is particularly true of patients with acute psychoses, of alcoholic patients, of suicide attempts, as well as patients with acute depressions or drug reactions and crisis in family reactions and personal adjustment. Emergency treatment is offered 24 hours a day at the emergency rooms of the three general hospitals in the area.

At the Connecticut Mental Health Center there will be a special 7-bed unit for emergency treatment and brief hospitalization. The major portal of entry to this unit will be through the emergency service of the general hospitals. In the case of Yale-New Haven Hospital, psychiatric residents from the Connecticut Mental Health Center will share the coverage of the hospital's Emergency Service with the psychiatric residents assigned to the hospital. Patients who are judged to need hospitalization at the Connecticut Mental Health Center, at the Connecticut Valley Hospital, or elsewhere, will be admitted to the 7-bed unit when beds are available for up to 72 hours to receive the benefits of diagnostic assessment, crisis intervention, and active psychiatric treatment. Considerable emphasis will be placed upon brief psychotherapy, drug treatment, involvement with the family, and relations to social agencies. It is hoped that the effective use of this facility will significantly reduce the number of patients from the area who are admitted to the psychiatric hospitals which serve the greater New Haven area.

#### **(3) OUT-PATIENT TREATMENT**

A large number of ambulatory patients with a wide variety of clinical disorders will be treated at the Connecticut Mental Health Center. In July, 1966, the Psychiatric Out-patient Clinic of the Yale-New Haven Hospital ceased to exist as a separate clinic and most of its functions will be absorbed by the Connecticut Mental Health Center. Treatment approaches will vary with the needs of the patients and the availability of staff. Most of the patients will be seen for relatively brief periods of time while a few may be seen for more intensive psychotherapy.



Depending upon their needs and our resources, patients will be treated in individual, group or family treatment, with or without the use of medication.

#### **(4) DAY HOSPITALIZATION**

One of the most successful recent trends has been the movement away from 24-hour bed care. The replacement of 24-hour care by day hospitalization or other partial hospitalization is increasingly common; the day hospital has emerged as a major facility for psychiatric treatment. The Day Hospital unit of the Center will serve as a direct admission unit, rather than being a transitional facility for patients previously hospitalized on the inpatient facilities. The Day Hospital unit will, therefore, admit selected patients referred directly from the community, the general hospital emergency departments, or the Connecticut Mental Health Center Emergency Treatment Service. It is estimated that 40-50 per cent of patients who previously were considered to require full-time inpatient care may be successfully treated on a day care basis. Day patients usually arrive at the hospital early in the morning and leave for home at 4 or 5 o'clock in the afternoon. Emphasis is usually placed upon the active participation of the patient's family in the therapeutic program.<sup>10</sup>

#### **(5) IN-PATIENT TREATMENT**

24-hour inpatient care is necessary for the management of acute episodes or crises as well as for patients with various forms of acute or chronic brain damage, severe suicidal or homicidal tendencies or major psychoses. However, in recent years the length of stay has been considerably reduced and the trend is toward shifting patients toward partial hospitalization or outpatient treatment.<sup>11</sup> Three 22-bed units (total of 66 beds) are available for in-patient care. These units will emphasize the intensive diagnostic assessment of a wide range of severe psychopathological conditions and the intensive treatment of patients with functional psychoses, different types of depressions, and severe neurotic disorders. Treatment emphasis will be varied: Individual psychotherapy, drug therapies and group and family treatment approaches will be integrated within the total social milieu. One of the units will be an intensive care and study facility closely integrated with programs of clinical and biological research.

#### **(6) AFTER-CARE AND REHABILITATION**

An important aspect of modern psychiatric care is the continuation of treatment efforts after the patient has been discharged from inpatient or day hospital care. Techniques of after-care have evolved to facilitate the patient's readjustment to

the community, to enhance his assumption of a productive vocational role and to assist him in his family relations. A program of rehabilitation will be developed to work closely with vocational rehabilitation services in the New Haven area.<sup>12</sup> We will also explore with the community the desirability and feasibility of special programs such as sheltered workshops, half-way houses, social clubs, and foster home placement. Under study is the possibility of joint programs between Center staff and those individuals engaged in occupational medicine.

#### **(7) CONSULTATION AND LIAISON WITH COMMUNITY AGENCIES**

Staff at the Connecticut Mental Health Center hope to integrate the Center's services into the larger New Haven community programs for health and social welfare. A consultation team composed of experienced members of the various mental health disciplines will be formed in order to provide ongoing liaison with community agencies, and, where appropriate, offer psychiatric consultation. Such a program is necessary to promote continuity of patient care. It is also important to facilitate inter-agency communication so that the Connecticut Mental Health Center can contribute to the over-all mental health planning for the greater New Haven region.

#### **(8) COMPREHENSIVE SERVICES TO A GEOGRAPHIC AREA**

A recent emphasis in community mental health programs has been the concept that the mental health facility must "reach out" into the community for early case finding and prevention. These efforts are still very new and their general utility is still under investigation. The Connecticut Mental Health Center will explore this approach with the hope of creating models of community psychiatry. Specifically, a geographic area within greater New Haven with a population of approximately 75,000-100,000 persons will be selected and assigned to a special service. Staff will undertake intensive neighborhood involvement including the development of one or more "field stations". This approach will supply important data for planning for the provision of the mental health services needed by the community as well as allowing for epidemiologic research.

#### **(9) SERVICES TO CHILDREN AND ADOLESCENTS**

Although no residential facilities have been constructed at the Connecticut Mental Health Center for the care of children and young adolescents, short-term hospitalization (up to one week) will be available in selected cases for assessment, evaluation and emergency treatment. In general, however, day hospital and inpatient care will be offered to patients over 18.

Outpatient services at the Center will ordinarily be available to persons over 16, but some children under 16 will be seen for diagnostic evaluation. Children of families whose adult members are being treated at the Center may be seen for evaluation and every effort will be made to insure that, where indicated, treatment programs will be located for such children. In the service or unit that offers comprehensive mental health services to a specific geographic catchment area, clinical services to children will be provided or located.

Close collaboration exists with the Yale Child Study Center whose child psychiatry program provides teaching, consultation and a community resource for long-term treatment. Psychiatric residents at the Center will participate in the child psychiatry training offered by the Yale Child Study Center as part of the Yale Psychiatric residency program.

### **The Organization Of The Center's Services**

In order to offer care to patients and training to students, three semi-autonomous general psychiatric Services will be organized. Each Service will be almost a sub-hospital that provides comprehensive care for patients, and training for mental health workers.

Each Service is based upon a facility, such as a 22-bed. Inpatient Unit, or the Day Hospital Unit. However, the clinical responsibilities and activities of the Service will extend beyond those patients in residential treatment; the Service teams will share coverage of the Yale-New Haven Hospital Emergency Service, offer treatment in the Center's 7-bed Emergency Treatment Unit, and jointly provide outpatient treatment.

In a modern mental health center only a small fraction of patients occupy beds. The modern psychiatric hospital is "a hospital without beds", as Sivadon put it.<sup>13</sup> Indeed one measure of the efficacy of modern clinical practice is the prevention of total hospitalization. Translated into quantitative terms, approximately 1,000 patients and their families will be served by the Center although fewer than 10 per cent will be "hospitalized" at any one time.

The development of the "unit system" has become a national trend in the past few years.<sup>14</sup> Large state hospitals have been operationally divided into smaller, semi-autonomous sub-hospitals that take responsibility for the comprehensive care of certain groups of patients (usually patients from a given geographic area). The functional organization of the Center is compatible with this trend. The three semi-autonomous general services at the Connecticut Mental Health Center will provide an administrative and clinical grouping that allows for flexibility and continuity both of patient care and

of teaching. This pattern is based upon certain general principles: (1) All three services will provide their own evaluation and diagnostic assessment. (2) All three services will accept direct admissions. Patients will remain on the unit to which they are admitted through treatment, convalescence and partial hospitalization, rehabilitation, and discharge. In the Day Hospital Unit, provisions for hospitalizing the small percentage of patients who may at times require 24-hour care will be made. (3) Each service will treat patients at all stages of illness. Therefore, there will be no distinction between closed, disturbed, admission wards, open, quiet or convalescent wards. (4) Each service will treat male and female patients. (5) Each clinical service will have one or more teams of professional and non-professional persons including medical, nursing, clinical psychology, occupational therapy, social work and related disciplines.

In addition to the general psychiatric services just described there are the Emergency Treatment Service, the Intensive Care and Study Facility and the Geographic Area Service. Outpatient services provided by the staffs of all the Services will be coordinated by an Outpatient Coordination team. The Rehabilitation Service and the Community Consultation Service consist of cadres of personnel experienced in these areas; they will be engaged in the development of programs and facilities that relate to patients' vocational and social rehabilitation, in carrying on programs of education and in consultation.

### **V. Training**

The Connecticut Mental Health Center will be a major training facility of the Yale University Department of Psychiatry. As a university facility, one of the major concerns of the Connecticut Mental Health Center will be the training of professional workers in psychiatry, nursing, social work and clinical psychology.

The most highly developed program at present is that of the training of psychiatric residents. First, second and third year residents (a total of about 18 residents in 1966-67) will receive training at the Center in general and social psychiatry. Some residents working in other hospitals of the State Department of Mental Health will be offered opportunities for training at the Connecticut Mental Health Center. Some of Yale's residents, particularly those in the administrative psychiatry program, will profit from full-time or part-time assignments to work in the other State institutions. Thus a closer and mutually beneficial relationship in training between the Connecticut Mental Health Center and the other hospitals of the State system may gradually be established.



Beginning in 1967-68, it is expected that the Center will play a very active role in the training of undergraduate medical students. The Center's programs will make it possible to expose them to a wide variety of approaches and techniques in general and social psychiatry and to offer them opportunities for research training in a number of disciplines and kinds of problems.

In social work, Yale has regularly had a number of trainees, most of them from the Smith College School of Social Work. With the Connecticut Mental Health Center as a training facility, the number of social work students at Yale will increase. The details of the training program in psychiatric nursing are being planned in concert with the Yale School of Nursing. Both pre-doctoral and post-doctoral students in clinical psychology will be trained at the Center.

**VI. Research**

At the Connecticut Mental Health Center, facilities will be available to allow the development of a multidimensional research program of high quality and promise.

The primary aim will be the development and organization of a research facility which can investigate problems in mental illness. The research residential unit, an Intensive Care and Study Facility, and the laboratories will be integrated into a unified functioning facility. Meaningful clinical studies can be carried out only when the personnel on the residential unit operate with the degree of awareness and precision that characterizes the laboratory scientist. To achieve this end, a considerable effort will be made to develop effective research teams consisting of physicians, nurses, and aides on the residential unit; and senior scientists, fellows, and technicians within the laboratories.

The second major research function of the Connecticut Mental Health Center will be to provide post-doctoral research training, as well as training of selected residents, in a research setting.

Research currently under consideration includes a variety of problem areas in a number of disciplines. Examples are: Biological studies of affective diseases; metabolic studies of psychomotor and temporal epilepsy; studies of subjective experiences in acute psychosis; the schizophrenic process in twins; and the organization and pathology of thought.

In the near future, studies of clinical psychopharmacological drugs used in the treatment of psychiatric illnesses are contemplated.

Of special importance are the projected studies on epidemiology and community psychiatry. This work will attempt to carry further the important Yale studies in social psychiatry.<sup>15,16</sup> The relation

of psychiatry and other mental health services to local community needs and resources and to social change will be the major focus of a research program in social and community psychiatry.<sup>17</sup>

Still another research focus will be the institution itself. Social scientists are expected to undertake studies on attitudes and roles of various mental health professionals and also on the communication process within the Center.<sup>18</sup>

**VII. Immediate And Future Planning**

To achieve the long-term aims and program goals that have been described, a systematic program for expansion over the next two years is planned, with services to be opened in the following order:

- (1) Outpatient Services
- (2) The Day Hospital Facility
- (3) The Emergency Treatment Service
- (4) An Inpatient Unit (22 beds)
- (5) Rehabilitation Service
- (6) Community Consultation Service
- (7) A field station of the Service offering Comprehensive Services to a Geographic Area
- (8) Intensive Care and Study Facility for Inpatients
- (9) Inpatient Service of the Geographic Area Service

As the program of the Connecticut Mental Health Center grows and develops, expansion of services within the Center will take place. The Center will also participate with other agencies in the community in the development of a comprehensive program offering a full range of mental health services.

The mental health problems of children, of adolescents and of the elderly are important areas of public concern. Together with other community agencies the Center will work toward the development of community programs for the alcoholic and for the geriatric patient, as well as toward systematic programs for children and adolescents. Center staff also plan to develop close working relations with the courts, the police and with the health and welfare agencies of the community.

**VIII. Afterword**

The program of the Connecticut Mental Health Center, whether it is viewed from the point of view of research or of patient care. The plans for clinical services and the research programs that have been described in this paper will evolve and will broaden into other areas of concern. Constant re-examination of goals and evaluation of the pathways to those goals will be undertaken by the staff. As a joint venture of the State of Connecticut and Yale University, the model-making role of the Connecticut Mental Health Center will continue

to be uppermost in the staff's thinking. Through the provision of excellent care for patients, training programs for mental health workers, and a vigorous program of research in all the disciplines that are related to mental illness and health, the Center will, it is hoped, make substantial contributions to the level of service, training and research.

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### PERSONAL PHYSICIAN

The internist is not, as some think, inclined to take over the function of personal physician from the receding general practitioner-family physician. The internist himself faces dissolution. Internal medicine keeps splintering itself into subspecialties—15 at the last count—and the divisions are self-sustaining and completely detached from the parent body. Most "internists" (physicians) now enter practice as performed "subspecialists" (specialists); others transform gradually from interest and emphasis in one area, to partial limitation of practice, and finally to full subspecialization. At this point of arrival the internist ceases to be an internist-personal physician with the entire patient as his province. He becomes a cardiologist or hematologist who is as far removed in name, function, and obligation to the full range and total conceptual import of internal medicine as the urologist. Ironically, in the process, the internist drags down with him into oblivion many a general practitioner, who, sensing the void generated by the departing internist and wishing to acquire specialty status, abandons general practice for internal medicine—a feat somewhat easily accomplished because of the similarities of the two fields and the nonrequirement of special technical skills. And given sufficient time, this transposed internist can likewise be expected to abdicate the ample confines of internal medicine for narrower and more compact terrain.—ZALE YANOF, M.D.



# THE PRESIDENT'S PAGE

## Regional Medical Programs

**A**MONG important measures dealing with Medicine, the 89th Congress enacted Public Law 89-239 authorizing federal grants to aid in planning and operating demonstration projects for the establishment of regional medical programs in the fields of heart disease, cancer, stroke and related diseases. This legislation, considered by many to have greater significance and potentiality than Medicare, was implemented on the basis of recommendations of a President's Commission (widely known as the DeBakey Report). Several amendments offered by an Advisory Committee of the A.M.A. were accepted before final adoption by Congress.

This bill aroused expressions of disapproval from various segments of the Profession. Some felt that its stated intent was too vague. The wisdom of establishing "categorical centers devoted to a single disease" was questioned. Others saw a threat to the existing time-honored role of the practicing physician in patient care. It was explained that lack of clearly defined methodology in the bill was an effort to permit flexibility of approach to fulfill needs which might vary with the regions. Good and bad experiences were cited where strict adherence to pooling of patients for specialized disease-management has been attempted in "categorized" private and military institutions. Departure from advantages offered by customary inter-departmental relationships is not an objective of the plan. Orientation of practice toward medical schools and hospitals was noted to be a definite trend, frequently with active support of physicians and the public, in urban communities. Medical schools, absorbed in research and training, are thought to be giving too little attention to the teaching and needs of the practitioner. It is believed that extension of continuing medical education and improvement of communications envisioned under the Regional Medical Programs will bring their "separate worlds closer together and permit each to learn from and assist the other."

The regional medical programs are intended to afford physicians and health institutions the opportunity to make available to their patients the latest advances in diagnosis and treatment of the designated diseases. To accomplish these purposes, the law proposes cooperative arrangements linking a region's health resources in programs of clinical research, education, training, and demonstrations of patient care. This is to be done without interfering with the patterns, or financing, of patient or professional care or with the administration of hospitals. Further elaboration of the details of the program is presented elsewhere in this issue of *Connecticut Medicine*.

On November 9, 1965 an ad hoc committee appointed by Governor Dempsey met and agreed to submit a plan for a regional medical program for Connecticut. The core of planning and development of the pilot project was assigned to the Yale University School of Medicine and the University of Connecticut School of Medicine with cooperative arrangements to include their affiliated teaching hospitals, the general hospitals, and other medical institutions throughout the entire State. Feasibility of the proposed plan was enhanced by the unique geographic nature of the State as a regional entity and realization of the considerable progress already made in the development of functional state-wide inter-hospital relationships. In June the application was approved by the National Advisory Council. Under requirement of the law, a broadly representative Advisory Board to assist in its implementation was appointed. This board includes voting members elected by four additional "Conference" groups which are described in an accompanying article in the *Journal*.

The State of Connecticut is fortunate to be one of the first four regions in the Nation to receive planning grants under P.L. 89-239. It is not without responsibility. The accomplishments of this pioneer project will receive wide scrutiny. We enter this exploratory phase of the program with confidence in the wisdom of those who will direct and supervise. Recognizing the value of early detection and the prevention, or delay of complications of the diseases under attack, preservation of the important role of the practicing physician with full provision of his needs at the local level should receive major consideration.

# **A Look At Public Law 89-239: The Heart Disease, Cancer, And Stroke Program**

**Arthur Ebbert, Jr., M.D.**

■ Public Law 89-239, known as the "Heart Disease, Cancer, and Stroke Amendments of 1965," has raised many questions for the medical profession and for those in related health fields. This article has been prepared to review the purposes and provisions of the law and to discuss planning to implement it in the State of Connecticut.

### **What Are The Objectives Of This New Law?**

The purposes as stated in section 900 of the legislation<sup>1</sup> are as follows:

"(a) Through grants, to encourage and assist in the establishment of regional cooperative arrangements among medical schools, research institutions, and hospitals for research and training (including continuing education) and for related demonstrations of patient care in the fields of heart disease, cancer, stroke, and related diseases;

"(b) To afford to the medical profession and the medical institutions of the Nation, through such cooperative arrangements, the opportunity of making available to their patients the latest advances in the diagnosis and treatment of these diseases; and

"(c) By these means, to improve generally the health manpower and facilities available to the Nation, and to accomplish these ends without interfering with the patterns, or the methods of financing, of patient care or professional practice, or with the administration of hospitals, and in cooperation with practicing physicians, medical center officials, hospital administrators, and representatives from appropriate voluntary health agencies."

### **Was There A Need For Such Legislation?**

The answer is yes if one acknowledges the gap between knowledge and technical skills which are available and knowledge and skills which are utilized in patient care. In recent years tremendous

progress has been made in diagnosis and treatment of heart disease, cancer, and stroke as in many other diseases. This progress through medical and other scientific research will undoubtedly continue at a rapid rate. A critical problem facing the medical profession is how these advances can be made readily and rapidly available to the practicing physician and in turn to his patients. This is a major objective of the legislation.

### **What Does The Law Provide?**

The law provides for grants "to assist public or nonprofit private universities, medical schools, research institutions, and other public or nonprofit private institutions and agencies in planning, in conducting feasibility studies, and in operating pilot projects for the establishment, of regional medical programs of research, training, and demonstration activities" for carrying out the purposes noted above. The term *regional medical program* is defined as "a cooperative arrangement among a group of public or nonprofit private institutions or agencies engaged in research, training, diagnosis, and treatment relating to heart disease, cancer, or stroke." Such a program must (1) be situated within an appropriate geographic area composed of part or parts of one or more states, (2) consist of one or more medical centers, one or more clinical research centers, and one or more hospitals, and (3) have in effect adequate cooperative arrangements among the various component units.

As noted by Kissick<sup>2</sup>: "The law encourages an alliance of public and private agencies and institutions to enable medical science, education, and service to join for the benefit of patients. The regional medical programs will aim to utilize more fully our existing facilities and trained manpower. The goal is economy and efficiency through improved community planning. The purpose of the program is to augment and enhance, rather than to supplant or duplicate existing manpower and facilities."

The law also supports education and training. This provides the opportunity not only for im-

*This article was prepared at the request of the Connecticut State Medical Society's Committee on Cooperation with the Medical Schools of Connecticut. The author acknowledges with sincere appreciation the encouragement and helpful suggestions received from members of that committee and from members of the Yale University School of Medicine—University of Connecticut School of Medicine ad hoc planning committee for the Connecticut Regional Medical Program.*

DR. ARTHUR EBBERT, JR., Associate Dean and Associate Professor of Medicine, Yale University School of Medicine, New Haven.



proved and expanded programs of continuing education for practicing physicians but also special training programs for individuals in the various health careers which are essential to support the physician.

Unfortunately, there has been considerable misunderstanding and confusion regarding the provisions of this new legislation.

It should be emphasized that the Heart Disease, Cancer, and Stroke Program has no relation to Public Law 89-97, the Social Security Amendments of 1965 known as "Medicare." It does not provide a government financed program of medical care. The law states that funds "shall not be available to pay the cost of hospital, medical, or other care of patients." The only exception is care related to the authorized research, training, or demonstration activities, and in such cases the law specifically requires that the patient be referred to the facility by a practicing physician.

Misunderstanding has resulted from the fact that the regional medical programs were originally referred to as "regional medical complexes." To some this erroneously suggested that specialized government health centers were to be established for the care of heart disease, cancer, and stroke patients. This is not the case. Existing health facilities are to join forces under the regional medical program. The law does not provide for new construction and existing facilities will not be duplicated.

Concern has been expressed by some who believed that the funds were designated for additional research on heart disease, cancer, and stroke. The law does not support basic research or clinical investigation; it is concerned solely with research in areas related to the stated purposes of the legislation, i.e., providing the most advanced clinical services on a regional basis and improving the utilization of existing health manpower and facilities.

A major advantage of this new federal program is that it recognizes the need for planning at the local regional level. It does not impose an already established program but instead promotes local initiative. Each region will differ in its existing facilities and in needs. Each region will have an opportunity to assess its assets and its needs and on this basis to plan its own regional medical program for the future.

#### **What Has Been Done In Connecticut To Implement This Law?**

Public Law 89-239 was signed by President Johnson on October 6, 1965. An ad hoc Committee on Heart Disease, Cancer, and Stroke appointed by Governor Dempsey met in Hartford on November 9 to consider this new federal legislation. The group

included representatives of the Connecticut State Medical Society, the Connecticut Hospital Association, and the State's two medical schools in addition to the Commissioner of Health and other prominent physicians and laymen. This committee agreed unanimously on the following proposals:

"1. There be one regional program for the entire state under the Heart Disease, Cancer, Stroke, and related diseases legislation.

"2. The planning and the program be based at the Yale School of Medicine and the University of Connecticut School of Medicine.

"3. The State Department of Health, State Medical Society and State Hospital Association will play leading roles on the Advisory Board, which would also include other institutional and individual representation as required by Section 903B4 of the legislation.

"4. The Yale School of Medicine and the School of Medicine of the University of Connecticut be designated as the institutions encouraged to apply for a federal grant to plan the Heart Disease, Cancer, and Stroke program for the State of Connecticut."

Thus the Governor's ad hoc committee, broadly representative of the State's health services, gave its support to the planning of a regional medical program and assigned the responsibility for this task to the two medical schools. During the next five months, the deans and selected faculty members of the schools of medicine at the University of Connecticut and Yale worked diligently in a series of meetings to prepare an application for a planning grant.

It was noted in this application that Connecticut possessed characteristics which made it an ideal area for the establishment of a regional medical program. The population of 2,825,000 is sufficient to require the full spectrum of medical facilities and yet is small enough to be served by a single coordinated program. There are excellent networks of transportation and communication within the State. The institutions required for a regional medical program already exist; in addition to the two medical schools, there are 35 accredited general hospitals and numerous active health agencies. Connecticut is fortunate in having well-trained medical personnel and excellent health facilities throughout the state, and the concept of planning, regionalization, and cooperative endeavor already is well established.

Early in the deliberations of this group charged with drafting an application for planning funds, it was decided that it would be advisable to have a single, all inclusive regional program for heart disease, cancer, stroke, and related diseases instead of three separate disease oriented programs. There-

fore, planning has been carried out on a noncategorical basis and will include all components covered by the legislation.

During this period when a Connecticut regional medical program application was being drafted, a New England Conference on Heart Disease, Cancer, and Stroke was considering the question of coordination of planning throughout the six New England states. Representatives of the two Connecticut medical schools and the Commissioner of Health met on several occasions with delegates from the other New England states. It was decided that planning grant applications would be submitted separately and independently by those groups which decided to do so and that each would develop its own planning program; however, in order to provide maximum coordination of all programs in the area, it has been proposed that a New England Committee for Regional Programs in Heart Disease, Cancer, and Stroke be established with two representatives from each of the participating states. This committee will provide a forum for coordination of activities and for exchange of information.

Public Law 89-239 requires that the applicant for a planning grant have an advisory group which includes "practicing physicians, medical center officials, hospital administrators, representatives from appropriate medical societies, voluntary health agencies, and representatives of other organizations, institutions, and agencies concerned with activities of the kind to be carried on under the program and members of the public familiar with the need for services provided under the program." This requirement presented a dilemma for those preparing the application because they envisioned an advisory group that would be small enough to be effective in formulating and supervising the plan for a regional medical program and yet large enough to be representative of all concerned. After considerable discussion and deliberation, a practical solution was found.

The Connecticut Advisory Board has been kept relatively small in a deliberate effort to make it a strong, influential, and efficient advisory group. It consists of fourteen voting members, including seven physicians (Table I). To have appointed representatives of each of the many institutions and organizations with a legitimate interest in the regional medical program would have resulted in an extremely large and unwieldy group with little opportunity to function effectively. Therefore, to encourage and facilitate participation and communication by all interested parties, four groups which will be called "Conferences" have been appointed to counsel and support the Advisory Board. These four Conferences are comprised as follows: (1) presidents of Connecticut hospitals, (2) chiefs of staff of Connecticut hospitals, (3) administrators

TABLE I  
MEMBERS OF THE ADVISORY BOARD FOR THE CONNECTICUT  
REGIONAL MEDICAL PROGRAM

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|                                                                                    |
|------------------------------------------------------------------------------------|
| Mr. Merlin D. Bishop, Hartford                                                     |
| Mrs. Herbert A. Brown, Bridgeport                                                  |
| Dr. Franklin M. Foote, Hartford                                                    |
| Dr. T. Stewart Hamilton, Hartford                                                  |
| Dr. Orvan W. Hess, New Haven                                                       |
| Dr. Stewart A. King, Stamford                                                      |
| Mr. James G. Pettit, Hartford                                                      |
| Mr. Arthur F. Rogers, Waterbury (Chairman)                                         |
| Dr. Bruce R. Valentine, Abington                                                   |
| Dr. John C. White, New Britain                                                     |
| Ex officio, with vote:                                                             |
| Chairman, Conference of Hospital Presidents—Mr. Frank T. Healy, Waterbury          |
| Chairman, Conference of Hospital Chiefs of Staff—Dr. Morris P. Pitock, Bridgeport  |
| Chairman, Conference of Hospital Administrators—Mr. Richard J. Hancock, New London |
| Chairman, Conference of State Health Organizations—To be elected                   |
| Ex officio, without vote:                                                          |
| Dean, University of Connecticut School of Medicine—Dr. John W. Patterson           |
| Dean, Yale University School of Medicine—Dr. Vernon W. Lippard                     |
| Director, University of Connecticut Hospital—Mr. John E. Ives                      |
| Executive Director, Yale-New Haven Hospital—Dr. Albert W. Snoko                    |

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of Connecticut hospitals, and (4) representatives of Connecticut health organizations. The chairman of each Conference is a voting member of the Advisory Board. It is apparent that every effort has been made to guarantee all interested parties will have a voice in the planning effort.

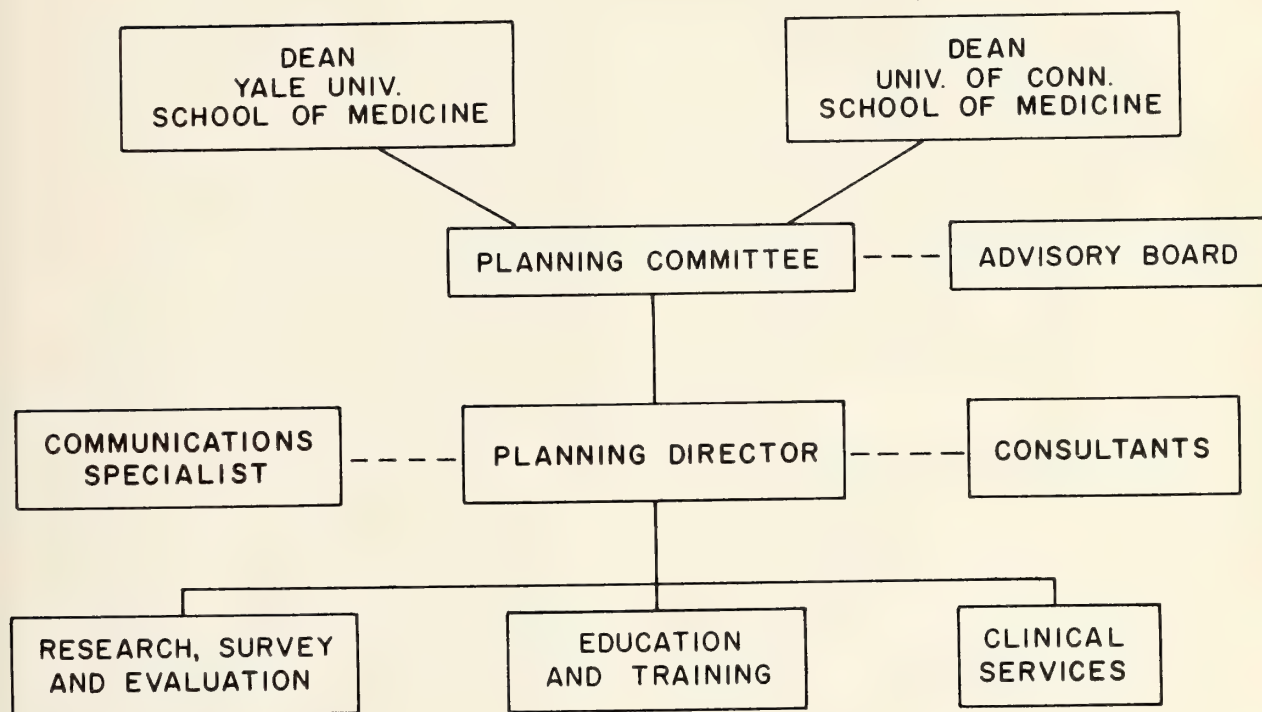
The Connecticut Advisory Board held its first meeting on April 15, and the proposed application was approved with some modifications. Although the four Conferences had not been activated at that time, these groups assembled in July for an initial orientation and discussion and to elect their chairmen. The application for a planning grant which had been submitted to the National Institutes of Health in April received final approval in June, and active planning will begin in the fall of 1966. It should be emphasized that the grant awarded by the National Institutes of Health is solely for planning and selected feasibility studies.

#### How Will The Planning Be Carried Out?

Planning a comprehensive and coordinated regional medical program presents a tremendous challenge. The goal is to develop a sound and workable proposal to establish and operate a continuing program which will make available to the people of the region the latest advances in diagnosis and



TABLE II  
THE PROPOSED TABLE OF ORGANIZATION  
FOR PLANNING THE CONNECTICUT  
REGIONAL MEDICAL PROGRAM



treatment of heart disease, cancer, stroke, and related diseases and to achieve maximal implementation and application of the research, training, and facilities which are currently available, or will become available in the future, for the care of patients with this broad spectrum of diseases. This will necessitate cooperative participation by practicing physicians and by numerous medical institutions and groups throughout the region including community hospitals, chronic care institutions and nursing homes, convalescent hospitals and rehabilitation facilities, the state and local health departments, voluntary health agencies, and various other professional organizations.

Planning will take a minimum of two years and will require the services of a director and staff who can devote their full time to this project (Table II). The director, a physician, will be concerned with the overall administration of the planning effort and will have as his primary responsibility the development of proposals for the future regional medical program. He will be guided by a

Planning Committee which will be concerned with policy matters. This committee and the director will be responsive to the counsel and guidance of the Advisory Board.

The activities of the planning staff will be organized in three separate but related areas: (1) research, survey, and evaluation; (2) education and training; and (3) clinical services.

The studies carried out under this program will be operational research and surveys designed to provide information on the present status of clinical and educational services and to determine existing and future needs and how they may be met. Such studies will be essential for planning and will also provide baselines for future evaluation of the effect of programs which eventually may be established.

Education and training are a most important aspect of the regional program and should include personnel in all the various health professions as well as practicing physicians and physicians in

specialty training. In this area, new educational and communication techniques must be explored.

With regard to clinical services, it is anticipated that the regional medical program will result in expansion of existing services and facilities and also development of new services and facilities to enable the practicing physician to function more efficiently and effectively and thereby to give improved patient care. A commonly cited example in this area is the establishment of intensive care units with physiological monitoring for patients with acute myocardial infarction and other life-threatening medical emergencies.

It is impossible to predict how the Connecticut regional medical program will evolve; however, it is anticipated that community hospitals will be the main centers for diagnosis and treatment and for education and training, with various special services and consultation available through the two university medical centers. It is important that the community hospital receive the support necessary to provide as many services as practicable in its own locale but have access to the unique facilities of the university centers for referral of special problems. At the same time, the community hospital should coordinate its activities and services with related institutions, agencies, and practicing physicians in the local area. Improved communication among all participants is considered essential for the success of such a program.

Thus the regional medical program may be envisioned as a series of six-lane highways between the university medical centers and key community hospitals providing traffic flow in both directions for clinical services, education and training, and continuing survey and evaluation. Each community hospital and medical center is also connected to related and supporting institutions and agencies by a network of subsidiary roads. As in major highway construction, utilization studies, surveys to determine present and future needs, close consultation among all parties concerned, and visionary planning are essential for the success of this program.

### **How Will The Program Benefit The Practicing Doctor?**

As noted previously, a major objective of Public Law 89-239 is to make the latest advances in diagnosis and treatment readily available to practicing physicians and in turn to their patients. As the regional medical program develops, this can be accomplished by providing the physician with information and with various services. Opportunities for innovations in these areas are tremendous.

Through improved and expanded programs of

continuing education and new communications techniques, the flow of information to the practicing physician can be greatly enhanced. Programs can be established whereby the doctor receives this information not only through conferences in his community hospital but also in his own office, at times when it is most needed and fits his working schedule.

There are many existing services and procedures which would be of considerable benefit to the doctor in his daily practice but which are not generally available at the present time. Many new services will undoubtedly develop from future technical and scientific progress. Some of these are services which the practicing physician will utilize in his own office; others can be made available to him in his community hospital or can be obtained through one of the major medical centers. The practicing doctor should also benefit from the development of expanded programs in the allied health professions; training programs for nurses, technicians, physical therapists, inhalation therapists, and other health personnel will make available services which are now difficult or impossible to obtain.

It should again be emphasized, however, that the present phase of the Connecticut regional medical program is one of planning. Through their participation in this planning effort and through their cooperation in the surveys and studies which will be necessary, practicing physicians will have an opportunity to define their needs and thereby to play an active role in the development of the future regional medical program.

### **Conclusion**

Connecticut is fortunate to be one of the first regions awarded a planning grant under Public Law 89-239. This provides a unique opportunity to study the health resources of the State with the purpose of determining present and future needs and planning a continuing, comprehensive regional medical program to meet these needs. Although the program concentrates on heart disease, cancer, stroke, and related diseases, these cover a broad spectrum of major health problems. Following the initial planning effort, it is hoped that feasibility studies and demonstration projects can be initiated in several areas as guides to further planning. This will require a cooperative environment in which all interested individuals and health organizations can contribute their ideas and work together toward the common goal of providing improved patient care.

This endeavor should encourage better communication and cooperation among the many health institutions and agencies, both private and



public, within the region with resulting improvement in the availability and use of health facilities, manpower, and services. This will be of direct benefit to the practicing doctor and will enable him to utilize new and more advanced clinical and technical developments in his daily practice.

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## IMPORTANT NOTICE

### CERTIFICATION AND RECERTIFICATION UNDER PART A OF MEDICARE

A considerable degree of confusion seems to exist among the nation's physicians about the required use of "special forms" to admit elderly patients to hospitals (certification) and to keep them there (recertification) under Part A of the Medicare Law.

In the "Reference Guide for Physicians," issued by the U. S. Department of Health, Education, and Welfare, it is stated (Page 19) that ". . ., it is *not* necessary for the certification or recertification statement to be entered on a special form."

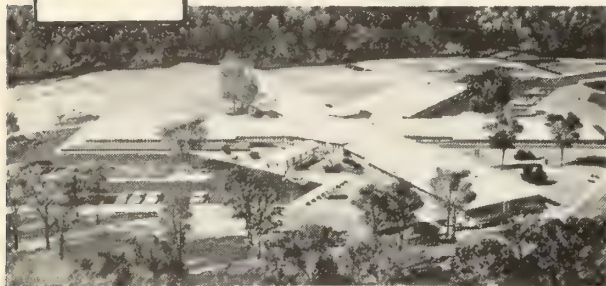
The American Medical Association has received reports, however, that some hospital administrations—for their own convenience and/or that of the fiscal intermediary—are insisting that staff physicians use special forms for these purposes. In a few instances, it appears that the forms are complex and that, to complete them, the attending doctors are being called upon to waste a great deal of time and effort.

In response to a question posed to him personally by Milton O. Rouse, M.D., President-Elect of the AMA, Mr. Arthur E. Hess, Director of the SSA Bureau of Health Insurance, replied:

"THE REFERENCE GUIDE FOR PHYSICIANS . . . EXPLAINS THAT A PHYSICIAN DOES NEED TO CERTIFY THE MEDICAL NECESSITY FOR ADMISSION AND TO RECERTIFY ON OR BEFORE 14 DAYS, AS WELL AS AT CERTAIN LATER INTERVALS. NO SPECIAL FORM IS REQUIRED, AND THE HOSPITAL DOES NOT NEED TO SEND THE CERTIFICATION TO THE INTERMEDIARY. THE SUBSTANCE COULD BE PART OF A RECORD THAT THE PHYSICIAN NORMALLY SIGNS IN CONNECTION WITH THE ADMISSION. TO THE EXTENT THAT THE NECESSARY INFORMATION IS CONTAINED IN AN ADEQUATE PROGRESS NOTE, THE THREE ITEMS TO BE COVERED IN RECERTIFICATION NEED NOT BE REPEATED. THUS, AN ADEQUATE ADMISSION OR PROGRESS NOTE WILL ITSELF SUFFICE IF IT STATES THAT THE INPATIENT SERVICES—OR CONTINUED SERVICES—ARE MEDICALLY NECESSARY AND IS SIGNED."

# W

## WESTFIELD NURSING HOME Inc.



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### CHRONIC or CONVALESCENT

- ALL MEDICAL CONDITIONS
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## RESOLUTION

### **SUBJECT: THE PRESCRIBING OF DRUGS UNDER THE MEDICAL ASSISTANCE (TITLE XIX) PROGRAM**

*Having received numerous protests concerning the regulations on the prescribing of drugs, as imposed by the Welfare Department in its July directive on the "Medical Assistance" program, on August 24 the Council adopted the following resolution which it will proceed to implement:*

WHEREAS: The attending physician assumes full professional responsibility for the medical care of his patients, irrespective of their economic status; and

WHEREAS: The prescribing of drugs, based on the physician's professional judgment, is an integral part of medical care; and

WHEREAS: The issuance of a prescription by the physician is, of itself, a "certificate of medical necessity"; and

WHEREAS: The Congress has declared its intent that persons entitled to benefits under tax-supported assistance programs shall receive medical care "of high quality, and in nowise inferior to that enjoyed by the rest of the populace"; therefore be it

RESOLVED: That the Council of the Connecticut State Medical Society strongly urge the State's Commissioner of Welfare to eliminate from the regulations governing Medical Assistance (the Title XIX program, if approved by HEW) all restrictions on the prescribing of drugs for MA beneficiaries which call for the attending physician to deviate from the usual practices he follows in rendering medical care to his other patients, or which disallow payment for drugs prescribed by a licensed physician; and be it further

RESOLVED: That the Commissioner of Welfare and the CSMS Advisory Committee to the State Commissioners of Welfare, Finance and Control be apprised of this action, and be requested to work cooperatively to implement its purposes.

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**PLEASE READ**

**IMPORTANT**

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## Around The State

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### CONNECTICUT MENTAL HEALTH CENTER DEDICATION CEREMONIES

September 30 – October 1

The recently constructed Connecticut Mental Health Center on 34 Park Street in New Haven will hold two days of ceremonies to dedicate the building, according to Dr. F. C. Redlich, Director of the new facility.

On Friday, September 30th, a large group is expected to attend the semi-public ceremonies which will be held on the steps and lawns of the Center. Governor John Dempsey, Yale President Kingman Brewster, and Commissioner of Mental Health Dr. Wilfred Bloomberg are scheduled to address the group, with New Haven Mayor Richard C. Lee presiding. Dr. John Donnelly, Chairman of the Connecticut Mental Health Board, and Mr. Andre Blumenthal, Chairman of the Center Advisory Board, will also be part of the program. Following the ribbon-cutting ceremony, scheduled tours and a reception are planned.

Friday evening, Mr. Wilbur Cohen, Under-secretary of Health, Education and Welfare will be the main speaker at a dinner for about 500 guests. Senator Abraham Ribicoff will introduce Mr. Cohen, and Dr. Francis Braceland will be toastmaster.

Saturday will be devoted to a series of scientific lectures with two central themes; morning, "The University and Community Mental Health", and afternoon, "Frontiers of Research". The morning session will be chaired by Yale Provost Charles H. Taylor, Jr., with University of Connecticut President Homer Babbidge, Development Administrator, Boston Redevelopment Authority, Edward J. Logue, and Dr. John Romano, Psychiatrist from University of Rochester as lecturers.

The afternoon session, at which Dean of Yale's School of Medicine will preside, will have as lecturers Dr. Neal Miller of Rockefeller University; Dr. Lawrence Kubie, Editor of *Journal of Nervous and Mental Disease*; Dr. Daniel X. Freedman, formerly of Yale and now at the University of Chicago Medical School; and Dr. Ernest M. Gruenberg, of Columbia University.

### News From Yale University School Of Medicine

Daniel J. Levinson, a prominent authority in the field of social psychology, has been appointed Professor of Psychology in the Department of Psychiatry at the Yale School of Medicine.

Formerly an assistant professor of psychology at the Harvard Medical School, Dr. Levinson was also director of the Center for Sociopsychological Research at the Massachusetts Mental Health Center.

In addition to his faculty appointment at Yale, Dr. Levinson will be Director of Behavioral Sciences at the Connecticut Mental Health Center which has just opened at the Yale-New Haven Medical Center.

Dr. Levinson has done extensive research on personality development and is recognized as an outstanding teacher. He is the co-author of two recent scholarly books, "Patienthood in the Mental Hospital," published in 1961, and "The Executive Role Constellation," published last year by the Division of Research of the Harvard Graduate School of Business Administration.

He was born in New York City on May 28, 1920. After receiving his B.A. and M.A. degrees from the University of California, he took his Ph.D. degree from that institution in 1947. For the next three years, he was assistant professor of psychology at Western Reserve University.

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Dr. Edward James Quilligan, Professor of Obstetrics and Gynecology at the University of California School of Medicine in Los Angeles, has been appointed Professor and Chairman of the Department of Obstetrics and Gynecology at the Yale School of Medicine.

An authority on fetal and maternal physiology, Dr. Quilligan has been Chief of Obstetrics and Gynecology at Harbor General Hospital, Torrance, California, for the past year, in addition to holding his academic appointment at U.C.L.A.

He will succeed Dr. C. Lee Buxton who has been on a leave of absence for several months because of illness. Dr. Buxton, who has headed Yale's Department of Obstetrics and Gynecology since 1954, is an internationally recognized specialist in his field and is best known for his work in advancing the cause of voluntary parenthood.



Dr. Quilligan's clinical background includes two years as Chairman and Director of the Department of Obstetrics and Gynecology at Cleveland Metropolitan General Hospital, from 1963 to 1965.

He is a member of the council of the Society for Gynecologic Investigation, as well as the council of the Association of Professors of Gynecology and Obstetrics, and a Fellow of the American College of Obstetricians and Gynecologists. In 1954 Dr. Quilligan shared with Dr. Charles Hendricks the Central Obstetrics and Gynecology Society Prize for their research on cardiac output during labor.

### **Third National Congress On Medical Quackery**

The Third National Congress on Medical Quackery will be held October 7-8 in Chicago (Pick-Congress Hotel).

The Congress will be sponsored by the American Medical Association and the National Health Council.

The Congress will bring together again major American groups concerned with efforts to safeguard the public against useless cures, mechanical gadgets, food fads and other quack devices and worthless treatment. The First National Congress on Medical Quackery was held in 1961 and the Second Congress was held in 1963.

The first two national congresses generated widespread interest in the need for education of the public against quackery, the AMA said. This interest has been translated into action at a state and community level. Quackery conferences have been held in many states and more are planned.

The quacks, put down in one area, keep showing up somewhere else with a new gadget or product, and there can be no letup in the campaign against them, the AMA declared. The Third National Congress will once again focus the full light of publicity and public opinion on quackery, which needlessly costs the American people an estimated billion dollars a year.

The theme of the three half-day sessions will be "Medical Quackery: 1966." Among speakers at the opening session will be James L. Goddard, M.D., commissioner of the U.S. Food and Drug Administration, "Drug and Device Quackery"; Ronald M. Deutsch, California author, "Nutritional Nonsense and Food Fanatics," and I. Frank Tullis, M.D., University of Tennessee professor of medicine, "Obesity: A Growing Problem."

A second session will include as speakers James Holland, M.D., of Roswell Park Memorial Institute, Buffalo, N.Y., "The Krebiozen Story: Is Cancer Quackery Dead?"; Mrs. Winthrop Rockefeller, president of the National Association for Mental

Health, "Mental Health and Psychological Counseling"; Robert J. Samp, M.D., of Madison, Wis., "A Look Inside Medicine's Own House"; Irving J. Ladimer, vice president of the National Better Business Bureau, "Literature and Advertising", and John W. Miner, chief of the medicolegal section of the Los Angeles County District Attorney's Office, "The Costs of Quackery."

The final session on October 8 will be devoted to chiropractic. Speakers will include Joseph E. Sabatier, Jr., M.D. of the AMA's Committee on Quackery, with a slide film documentary; Eugene Robillard, M.D., associate dean of the Faculty of Medicine of the University of Montreal, "A Survey of Chiropractic", and H. Thomas Ballantine, Jr., M.D., of Massachusetts General Hospital and Harvard Medical School, "Medicine and Chiropractic."

### **New Director Of World Health Organization**

Dr. Alfred E. Evans has been appointed as the new director of the World Health Organization (W.H.O.) Reference Serum Bank in the United States which is located in the Department of Epidemiology and Public Health, Yale University School of Medicine, New Haven, Connecticut. The functions of the W.H.O. Serum Banks consist of the analyses of information obtained from serologic surveys, and the storage of collections of sera which are useful in determining patterns of antibodies and various blood components, including those of significance in the field of population genetics.

### **New Haven County**

The 183rd Semi-Annual Meeting of the New Haven County Medical Association has been scheduled for Thursday, October 27, 1966 at the Waverly Inn, Cheshire, Connecticut. The Business Session is scheduled to begin at 3:30 P.M. The speaker of the evening is Mr. Bernard D. Hirsh, L.L.B. of the A.M.A.

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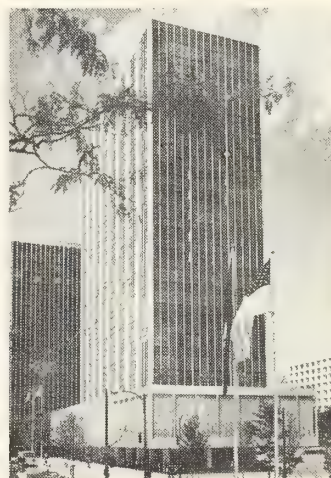
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## 1966 MEETINGS

**September 28** — 41st Connecticut Clinical Congress to be held at Mary S. Harkness Auditorium, Yale University Medical School, New Haven, Connecticut. The program will be devoted to "Recent Advances in the Diagnosis and Management of Liver Disease" and "Recent Advances in the Diagnosis and Management of Thrombophlebitis."

**September 29-30**—Seminar on Diabetes. Deauville Hotel, Miami Beach, Florida. G. F. Cahill, S. S. Fajans, W. J. Harrington, A. G. Hills, E. C. Miller, M. Siperstein, W. C. Thomas, will be guest speakers. Florida Diabetes Association, R. T. Rengarts, M.D., Secretary, P.O. Box 268, Sebring, Florida 33870.

**October 27** — 183rd Semi-Annual Meeting of New Haven County Medical Association to be held at Waverly Inn, Cheshire, Connecticut at 3:30 P.M.

## 1967 MEETINGS

**January 17-19** — New England Postgraduate Assembly will be held at the Statler Hilton Hotel, Boston, Massachusetts. Advance Program will be sent in early December.

**April 12-13**—Seminar on Hospital Infections in Connecticut to be sponsored jointly by the Connecticut State Medical Society, Connecticut Hospital Association, Yale University School of Medicine, the Connecticut State Department of Health and the Communicable Disease Center of the Public Health Service.

**April 25-27** — 175th Annual Meeting of the Connecticut State Medical Society to be held at the Statler-Hilton Hotel, Hartford, Connecticut.

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## **Heredity And Environment In Leukemia And Lymphoma**

A group of Nebraska families has been identified in which the malignant diseases leukemia and lymphoma occur two and a half times as frequently as in a control group from the same area.

This suggests that susceptibility to these somewhat similar diseases may be inherited, says an article in the current *Journal of the American Medical Association*.

The authors point out that it is susceptibility to a disease that may be inherited—not the disease itself.

Viruses, pneumonia-like organisms, and other infectious agents have all been suspected as causes of human leukemia and lymphoma. Animals have been implicated as the carriers of these infectious agents.

The four physician-investigators from the University of Nebraska College of Medicine and the Eppley Institute for Cancer Research, Omaha, interviewed 92 families (with 1,532 members) in which at least one person had leukemia or lymphoma. They also interviewed 69 randomly selected families with 1,294 members; some of these contained leukemia-lymphoma victims, others did not.

All of the families were from rural, eastern Nebraska, and all shared a common characteristic: considerable association with farm animals. The investigators reasoned that if animal-carried agents are involved in leukemia and lymphoma, both study groups would have similar exposure.

It was relatively easy to trace family histories for several generations in the stable, close-knit farm communities, the physicians said.

They found evidence of malignancies in most of the families, but leukemia and lymphoma appeared two and a half times as often in families in which at least one other member was known to have had the disease.

Twenty-one families were found with "multiple involvement," meaning two or more cases of leukemia or lymphoma. Forty-nine persons in these families had one or the other of the diseases, and 76 additional relatives had other malignant diseases.

Thus, in the "high risk" families, 125 out of 544 members (23 percent) were found to have suffered some kind of malignant disease. Among 71 persons whose families contained only one known case of lymphoma or leukemia, 41 had at least one blood relative with a diagnosis of other malignancy (148 of 988 family members, or 15 per cent).

Forty-nine of the 69 control families had at least one member with a diagnosis of malignancy (132 of 1,294 family members, or 12 per cent).

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## In Memoriam

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**Backer, Marcus** — Bridgeport; Yale University School of Medicine, 1924. Dr. Backer was a heart specialist in the Bridgeport area for many years. During the 1930's, he opened a free heart clinic in Fairfield, one of the first in the state. He was a consultant at St. Vincent's Hospital and an assistant professor of clinical medicine at the Yale University School of Medicine. He was a member of the Fairfield County Medical Association, the Connecticut State Medical Society, and the American Medical Association. Dr. Backer died August 4, at the age of 70.

**Ferrell, Ernest H., Jr.**—Woodbridge; Western Reserve University Medical School, 1947. Dr. Ferrell was a member of the New Haven Medical Society, the New Haven County Medical Association, the Connecticut State Medical Society, and the American Medical Association. He was a fellow of the American Board of Surgeons. Dr. Ferrell died July 13, at the age of 42.

**Groark, Owen J.** — Bridgeport; Medico-Chi Medical School of Philadelphia, 1916. Dr. Groark was a practicing physician in Bridgeport for 50 years. During World War I, he served as a first lieutenant with the Army Medical Corps in France and Germany. Dr. Groark was a former president of the Bridgeport Medical Society. For 25 years, Dr. Groark served as director of the radiology department at St. Vincent's Hospital and later served as consulting roentgenologist for the hospital. He was a member of the Bridgeport Medical Society, the Fairfield County Medical Association, the Connecticut State Medical Society, the American Medical Association, and the Radiological Society of North America. He was a diplomate of the American College of Radiology and the American Board of Radiology. Dr. Groark died July 27, at the age of 75.

**MacLeod, Edith A.**—Niantic; Women's Medical College of Pennsylvania, 1925. Dr. MacLeod was the medical director at the Niantic State Farm and Prison for Women for 23 years. She was a member of the New London County Medical Association, the Connecticut State Medical Society, and the American Medical Association. She was a former director of the Niantic Nursing Association. Dr. MacLeod died June 25, at the age of 68.

**Reynolds, Harry S.**—Ellington; Albany Medical College, 1914. Dr. Reynolds was a general practitioner in West Hartford for 47 years, with a specialty in dermatology. During World War I, he served as a lieutenant in the Army Medical Corps. A member of the Dermatological Service of St. Francis Hospital, he was a visiting consultant at Hartford Hospital; Manchester Memorial Hospital; Day-Kimball Hospital, Putnam; Winsted Hospital, and the Charlotte Hungerford Hospital, Torrington. He was a member of the Hartford County Medical Association, the Connecticut State Medical Society, the American Medical Association, the New York Academy of Medicine, and the New England Dermatological Society. Dr. Reynolds died August 1, at the age of 77.

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## Doctor's Office

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John Burbank, M.D., Michael J. Esposito, M.D., and John F. Hennessey, M.D. announce the association with them of Carl W. Scheer, M.D. in the practice of radiology at 26 Fair Street, Wallingford, 335 Cook Avenue, Meriden, and 350 South Main Street, Cheshire.

Max G. Carter, M.D., George L. Wilson, M.D., Philip R. Fazzone, M.D., and Donald S. Dock, M.D., announce their association in the practice of thoracic and cardiovascular surgery at 670 George Street, New Haven.

Jerome T. Combs, M.D., announces his association with Anthony Piccirillo, M.D. and Delbert B. Smith, M.D. in the practice of pediatrics at 45 Fair Street, Wallingford.

Harris Cantor Faigel, M.D., announces the opening of an office for the practice of adolescent medicine at 123 York Street, New Haven.

Robert Fand, M.D., announces the opening of an office for the practice of dermatology at 8 West Street, Danbury.

Malcolm Gorin, M.D., announces the opening of an office for the practice of general eye care and eye surgery at 40 Broad Street, Middletown.

Robert E. Hicks, M.D., announces the opening of an office for the practice of surgery and reconstructural surgery at 233 Main Street, New Britain.

John T. DeMaio, M.D., announces the opening of an office for the practice of general surgery at 283 Collins Street, Hartford, in association with Dr. Deal T. Aseltine, Jr.



## PLACEMENT WANTED

G.P.—with 2 years training in Internal Medicine, 8 years practice in medicine, wishes opportunity as associate in Southern Conn. Will consider salaried position leading to partnership or position in Industrial Medicine or a hospital appointment.

OBS-GYN—35 years of age, Board eligible, military obligations completed. University trained, would like to form either an association or join a group practice.

ANESTHESIOLOGIST—40 years of age, Board eligible, Connecticut license. Military obligations completed, would like to associate with another physician or practice in an institution.

INTERNIST—29 years of age, married, Board eligible. Would like to practice in either a solo or partnership situation within easy traveling distance of New York.

PEDIATRICIAN—37 year old Board eligible pediatrician with background in general pediatrics and pediatric oncology desires to associate with other pediatricians in New Haven area. Military obligations completed.

## PLACEMENT OPPORTUNITIES

WANTED: General Practitioner or Internist for General Medical and Surgical Accredited State Veterans' Hospital. Duties are those of ward officer on a medical ward. Older physicians acceptable, many fringe benefits, such as housing and maintenance, are at minimal cost. Salary range \$13,040 to \$17,040. Apply: Personnel Officer, State Veterans Home and Hospital, Rocky Hill, Connecticut.

PSYCHIATRIST needed for a community-oriented mental hospital, to direct service within a 300-bed State mental hospital. Opportunity for teaching, clinical work and research. Has to develop and direct team of social workers, psychiatric residents, psychologists and more than 80 nursing staff personnel. O.P.D., day care, in-patient consultation and emergency care available. Opportunity for association with Wesleyan, Yale and University of Conn. Salary: \$14,240-\$20,000, depending on qualifications and experience. Excellent fringe benefits and annual leave to attend medical conventions. All particulars should be in first letter, including references. Apply—John F.

Lowney, Jr., M.D., Supt., Connecticut Valley Hospital, Box 351, Middletown, Conn. 06458.

PATHOLOGIST—full-time or half-time to direct clinical laboratory in 2300-bed mental hospital. Ample opportunity for research and teaching available. Well equipped and staffed laboratory, emphasis on neuropathology. Board certified or eligible pathologist preferred. Salary: \$14,740-\$19,000. Excellent fringe benefits. All particulars and references should be sent in first letter. Contact—John F. Lowney, Jr., M.D., Supt., Connecticut Valley Hospital, Box 351, Middletown, Conn. 06458.

CLINICAL DIRECTOR to develop medical program in psychiatric hospital with emphasis on psychosomatic medicine. Opportunity for experience in employees' health clinic, workmen's compensation, clinic and psychopharmacologic drug research. Will direct department staffed by seven physicians. EEG, EKG, Radiology, Ophthalmology Depts. already fully equipped and staffed. Consultants available in all medical and psychiatric specialties. Salary: \$15,460-\$20,000, excellent fringe benefits, annual leave to attend medical conventions. All particulars and references should be included in first letter. Apply—John F. Lowney, Jr., M.D., Supt., Connecticut Valley Hospital, Box 351, Middletown, Conn. 06458.

CLINICAL PHARMACOLOGIST — Physician who wants to combine medical knowledge, scientific inquisitiveness and administrative skills. Highly desirable are previous experience in pharmaceutical industry, background of private practice and some type of specialized medical training, although a strength in one area may outweigh a lack in the others. As a member of the Research Div., he will be active in the planning of new medicinal research programs. Between 10% and 20% of the time, the physician will be on scientific field trips or attending various professional meetings, but will rarely be gone for more than three consecutive days. Members of the Clinical Pharmacology Dept. are encouraged to publish scientific papers based on their own studies. Contact: D. V. Vines, Personnel Mgr., Chas. Pfizer & Co., Inc., Groton, Conn., 06340.

ANYONE INTERESTED IN THE ABOVE IS ASKED TO CONTACT THE GENERAL MANAGER'S OFFICE, 160 ST. RONAN STREET, NEW HAVEN, CONN. 06511.

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## Special Notices

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### SEMINAR ON "DIGITALIS AND THE HEART"

October 15 and 16, 1966

A Seminar on "Digitalis and the Heart", October 15 and 16, 1966, will be presented at the DeGoesbriand Memorial Hospital in Burlington, Vermont, sponsored by the Vermont Heart Association and the University of Vermont in collaboration with the American College of Cardiology. Programs may be obtained by writing Eugene Lepeschkin, M.D., Cardiovascular Research Unit, DeGoesbriand Memorial Hospital. The speakers will include Charles Fisch, M.D., Professor of Medicine at Indiana University, Niels Haugaard, Ph.D., Assoc. Professor of Pharmacology at the University of Pennsylvania and faculty members of the University of Vermont.

### MOUND PARK HOSPITAL FOUNDATION, INC.

October 20-22, 1966

Symposium on "Industrial Medicine: The Doctor's Role in Occupational Health." Mound Park Hospital Foundation, Department of Medical Education of the Mound Park Hospital, Bay Pines V. A. Hospital, Pinellas County Medical Society, University of South Florida Division of Continuing Education, American Academy of General Practice—October 20 to 22, 1966, inclusive. The Foundation reserves the right to limit registration. Fee \$40.00. 18 Accredited Hours by the American Academy of General Practice. Address: Industrial Medicine, Mound Park Hospital Foundation, Inc., St. Petersburg, Florida 33701.

### TWO AND ONE-HALF DAY SYMPOSIUM ON EPILEPSY

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### TWO-DAY COURSE IN ORAL CANCER AND ORAL CYTOLOGY

October 20 and 27, 1966

A two-day course in Oral Cancer and Oral Cytology is being sponsored by the Connecticut State Dental Association and Connecticut State Department of Health at Holiday Inn, Meriden, Conn., on Thursday, October 20 and 27, 1966.

This being the final two-day course to be presented prior to the termination of the Oral Cancer Project in August 1967,

we invite all physicians to attend, and urgently suggest they take advantage of this opportunity.

The purpose of the course is to demonstrate to dentists and physicians throughout the state, the newest concepts in oral cancer detection and management, the primary goal being to reduce the number of deaths resulting from oral cancer each year.

Project directors are Dr. Ronald Voglesong, Chief, Dental Health Section, Connecticut State Department of Health, 79 Elm Street, Hartford, Conn., and Dr. Robert H. Bernert, Hartford.

If interested in taking the course, please contact Dr. Voglesong.

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## Letter To The Editor

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### To The Editor:

What a delightful surprise it was to find the Handel biographical note on page 508 of the July, 1966 issue of *CONNECTICUT MEDICINE* under the heading, "The Mind of a Genius." May I take a moment to correct certain inaccuracies?

No less an authority than the composer himself selected appropriate spelling for his Christian names and the omission of the Germanic umlaut from the family name. Thus he signed his name, from the time he settled permanently in England, George Frideric Handel.

Unfortunately the canard that a curate named Pooley, presumably Jennens' secretary, wrote the libretto of *Messiah*, rather than Charles Jennens, is repeated. Only Hone in his *Table Books*, Vol. III, names Pooley as the true author; even Newman Flower recanted on this point. More recent research has failed to reveal any man named Pooley in contemporary clergy lists, nor in any material associated with Jennens. Hone remains the single author to attribute *Messiah* to anyone but Jennens.

The oratorio is properly named *Messiah*, although on at least two occasions Handel himself referred to it as *The Messiah*—in a letter to Jennens on September 9, 1742 and again in a letter dated July 19, 1744. The autograph in the British Museum is titled *Messiah*. Interestingly, the oratorio was presented merely as *A Sacred Oratorio* in order to assuage the ecclesiastic authorities in London. Whatever it may be called, this work stands in rarefied air in the company of Bach's *St. Matthew Passion* and Verdi's *Manzoni Requiem*.

It may be of interest that Handel was often racked with intense and disabling arthritic pain, possibly gouty, in his right arm and leg, almost to the point of disuse. Yet less than two weeks after his 74th birthday, in a fabulously successful concert season, he performed *Messiah* on April 6, 1759, totally blind. Eight days later he died, on Holy Saturday—a day late for his own wish to join his Savior on the day of his Resurrection.

Yours truly,

HOWARD K. ENTE, M.D.

Westport, Connecticut

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**Precautions:** Use with caution in patients hypersensitive to sympathomimetic compounds, who have coronary or cardiovascular disease, or are severely hypertensive.

Dextro-amphetamine sulfate: Excessive use by unstable individuals may result in psychological dependence.

Meprobamate: Careful supervision of dose and amounts prescribed is advised, especially for patients with known propensity for taking excessive quantities of drugs. Excessive and prolonged use in susceptible persons, e.g. alcoholics, former addicts, and other severe psychoneurotics, has been reported to result in dependence on the drug. Where excessive dosage has continued for weeks or months, reduce dosage gradually. Sudden withdrawal may precipitate recurrence of preexisting symptoms such as anxiety, anorexia, or insomnia; or withdrawal reactions such as vomiting, ataxia, tremors, muscle twitching and, rarely, epileptiform seizures. Should meprobamate cause drowsiness or visual disturbances, reduce dosage and avoid operation of motor vehicles, machinery or other activity requiring alertness. Effects of excessive alcohol consumption may be increased by meprobamate. Appropriate caution is recommended with patients prone to excessive drinking. In patients prone to both petit and grand mal epilepsy meprobamate may precipitate grand mal attacks. Prescribe cautiously and in small quantities to patients with suicidal tendencies. **Side Effects:** Overstimulation of the central nervous system, jitteriness and insomnia or drowsiness.

Dextro-amphetamine sulfate: Insomnia, excitability, and increased motor activity are common and ordinarily mild side effects. Confusion, anxiety, aggressiveness, increased libido, and hallucinations have also been observed, especially in mentally ill patients. Rebound fatigue and depression may follow central stimulation. Other effects may include dry mouth, anorexia, nausea, vomiting, diarrhea, and increased cardiovascular reactivity.

Meprobamate: Drowsiness may occur and can be associated with ataxia; the symptom can usually be controlled by decreasing the dose, or by concomitant administration of central stimulants. Allergic or idiosyncratic reactions: maculopapular rash, acute nonthrombocytopenic purpura with petechiae, ecchymoses, peripheral edema and fever, transient leukopenia. A case of fatal bullous dermatitis, following administration of meprobamate and prednisolone, has been reported. Hypersensitivity has produced fever, fainting spells, angioneurotic edema, bronchial spasms, hypotensive crises (1 fatal case), anuria, stomatitis, proctitis (1 case), anaphylaxis, agranulocytosis and thrombocytopenic purpura, and a fatal instance of aplastic anemia, but only when other drugs known to elicit these conditions were given concomitantly. Fast EEG activity, usually after excessive dosage. Impairment of visual accommodation. Massive overdosage may produce drowsiness, lethargy, stupor, ataxia, coma, shock, vasomotor and respiratory collapse.



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## NEW BOOKS IN REVIEW

**INDEX-HANDBOOK OF CARDIOVASCULAR AGENTS 1956-1959. Volume 3. Isaac D. Welt, Institute for Advancement of Medical Communication. McGraw Hill Book Co., New York, 1965. 1235 pp. \$32.50.**

Reviewed by: LOUIS H. NAHUM

In this book, Volume 3 of the series 11000 scientific communications published between 1956-1959, are analyzed and annotated with reference to the various drugs involved in their actions on the cardiovascular system. It is comprehensive and penetrating. Generally a title of a scientific paper gives no indication of the drugs to which reference is being made nor to the data concerning their biological effects. These troublesome omissions are overcome by analysis in depth through indexing and cross-indexing. As a result prompt reference can be obtained with regard to the characteristics of the action of the drug under consideration.

The raw data for this Cardiovascular Literature Project come from 398 medical and scientific periodicals, published throughout the world in a score of languages. Detailed lengthy and informative index entries alphabetically labelled, it is here shown, can largely replace conventional abstracts for most applications. With minor modifications this technique should be able to be extended to include coverage of chemical effects upon any number of well recognized biological entities. In other words, the method used by Dr. Isaac D. Welt in this volume is well suited to the indexing of the entire literature of fundamental pharmacology as well as that of applied therapeutics.

This volume may be considered as a valuable working experiment. Its success holds promise of opening a new field in scientific documentation. One result as Dr. Chauncey Leake states in his preface, might be that indexes to scientific literature may become significant intellectual analytic tools.

This book should of course be in every library, and every basic biomedical science department. It will help to save much time for the scientist who is beset with the problem of retrieving pertinent information and free him to pursue his scientific investigations. In this sense, Dr. Welt has made a fundamental contribution to scientific progress.

**CIBA FOUNDATION STUDY GROUP NO. 22. GONADOTROPHINS: Physico-chemical and Immunological Properties. G. E. W. Wolstenholme, O.B.E. and Julie Knight, B.A. Little, Brown & Co., Boston, 1965. Thirteen contributors. 125 pp. with 28 illustrations. \$3.50.**

Reviewed by: LOUIS H. NAHUM

This little volume begins with an excellent historical introduction of the subject by Christian Hamburger in whose honor this Ciba Symposium was organized. The background of the meeting is the fact that we are entering an immunological era which has opened the way for making immunological determinations of the gonadotropins which are protein in character. To do this we need highly purified hormones which make possible an understanding of physicochemical

structure. This book then is devoted to methods of preparation of such purified hormones. Thus we find an easy reference to the latest literature as well as methods of purification and bio-assay as well as the actions of the gonadotropins as antigens. There is a learned discussion at the end by C. J. O. R. Morris. It is obvious the book is for basic scientists, of an endocrinological and physicochemical orientation.

**HYSTERIA: The History Of A Disease, by Ilza Veith. The University of Chicago Press, Chicago, 1965. 301 pp. Illustrated. \$7.95.**

Reviewed by STEPHEN FLECK

This is a very interesting well-written book, but hardly a history of hysteria. The author's broad knowledge of the history of medicine in all parts of the world, and through the ages shines, but her lack of depth in historical scholarship and in psychiatric matters glares. As history the book is anecdotal rather than thematic, and extensive discursions which characterize the earlier chapters, such as biographical sketches of the various writers on the subject, are no substitute for essential data on the socio-cultural context and perspectives in which a particular treatise cited should be placed for historical appreciation. However, these earlier chapters are interesting refreshers for the non-student of medical history, and the last few chapters may be of interest also to the non-psychiatrist. For the psychiatrist, this is a book of missed opportunities.

The author questions the elimination of hysteria as a disease in the preface, and seems oblivious to the fact that much of what has been called hysteria through the ages is now assigned to other diagnostic categories, but, of course, hysteria has not been eliminated in substance, not from the nomenclature, nor from clinical communicative usage, and least of all from clinical purview as the author claims at the book's end. This omission of the post-Freudian history of hysteria, its reappearance on neurological services, and its re-examination in the light of social and transactional psychiatry renders the book particularly unsatisfactory. Rush, a century ago, observed that "the hysterical and hypochondriac disorders once peculiar to the chambers of the great are now to be found in our kitchens and workshops." (An Account of the Influence of the American Revolution upon the Human Body" in Medical Inquiries and Observations. Phila. 1809, Hopkins and Earle). This observation offers just one of the very many opportunities for further historical investigation, such as the evolution of thought and concept on social factors in medicine through the ages. Or, the intriguing questions of why so many outstanding observers, scientists, and clinicians including Harvey, Sydenham, and Charcot himself, while astute in describing such patients, emphasizing or deemphasizing the sexual elements, allowed their critical faculties to go so far afield and let themselves be governed by folklore and traditional shibboleths? These are but two examples of many thematic pursuits suggested by the material, which would be important to the psychiatrist and worthy of a historian's mettle.



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**PHYSICAL EXAMINATION OF THE JOINTS.** by William P. Beetham, M.D., Howard F. Polley, M.D., Charles H. Slocumb, M.D., and Walt F. Weaver, M.D. The W. B. Saunders Company, Philadelphia and London, 1965. 198 pp. Illustrated. \$7.50.

Reviewed by: HUGH F. LENA

This book is a short, practical, comprehensive guide for the examination of the joints written by four specialists in rheumatic diseases at the Mayo Clinic and Graduate School of Medicine. The American Rheumatism Association's nomenclature and classification of arthritis and rheumatism is presented. A careful description of joints is given. The three main types are the synarthroses, or immovable articulations; the amphiarthroses or slightly movable articulations; and the diarthroses, or freely movable articulations. A detailed description is also given of the seven forms of articulating surfaces: plane, spheroidal, cotylic, hinge, condylar, trochoid, and sellar.

The entire emphasis is on the precise systematic performance of joint examination. Swelling about a joint may be caused by intra articular effusion, synovial thickening, peri-articular soft-tissue inflammation such as bursitis or tendinitis, bony enlargement, or extra-articular fat pads. These conditions must be carefully differentiated from one another. The synovial membrane is the soft tissue of the joint and is commonly inflamed or involved by a disease process very early. The anatomy of the synovial membrane is described in detail since changes may be detected by careful physical

examination earlier than the involvement of the hard articular structures.

The range of motion of a joint is emphasized. The authors feel that active range of motion should always be observed before the passive range of motion is determined whenever possible. An ingenious joint chart is employed at the Mayo Clinic. This utilizes abbreviations of the joints to avoid a cumbersome chart and contains three columns for swelling, tenderness and limitation of motion. It is suggested that a system of grades be used from 0 to 4 in which 0 signifies normal and 4, maximally abnormal.

There is a separate chapter devoted to each joint, from the temporomandibular joint to the joints of the feet. The joint is described according to the essential anatomy, inspection, palpation, movement, range of motion tests, and referred pain. Clinical photographs are included in every chapter. The anatomical drawings are especially helpful and in many of these the synovial membrane is shown in blue color to emphasize its importance and its relation to other structures.

The material is arranged according to objective signs and is concerned primarily with the recognition and localization of disease. The diagnostic classification of disease is not emphasized. This monograph would be helpful, not only to rheumatologists, but also to orthopedists, internists and general physicians.

## BOOKS RECEIVED

*Books received for review are acknowledged in this department and such acknowledgement must be regarded as a sufficient return for the courtesy of the sender. Selection will be made for review in the interests of our readers and as space permits.*

*Orthotics Etcetera.* The ninth volume of Physical Medicine Library. Edited by Sidney Licht, M.D., assisted by Herman L. Kamenetz, M.D. with 26 contributors. Elizabeth Licht, Publisher, 1966. 774 pp. \$24.00.

*Arteriography.* Principles and Techniques Emphasizing Its Application in Community Hospital Practice. Joseph L. Curry, M.D. and Willard J. Howland, M.D. W. B. Saunders Co., Philadelphia and London, 1966. 328 pp. Illustrated. \$14.00.

*Operable Heart Disease.* Pathophysiology, diagnosis, and treatment. Howard D. Sirak, M.D. The C. V. Mosby Company, St. Louis, 1966. 130 pp. Illustrated. \$12.50.

*Clinical Epidemiology.* Revised Edition by John R. Paul. The University of Chicago Press, Chicago and London, 1966. 305 pp. \$7.50.

*The Theory And Practice Of Psychiatry.* Frederick C. Redlich and Daniel X. Freedman. Basic Books, New York, 1966. 880 pp. \$12.50.

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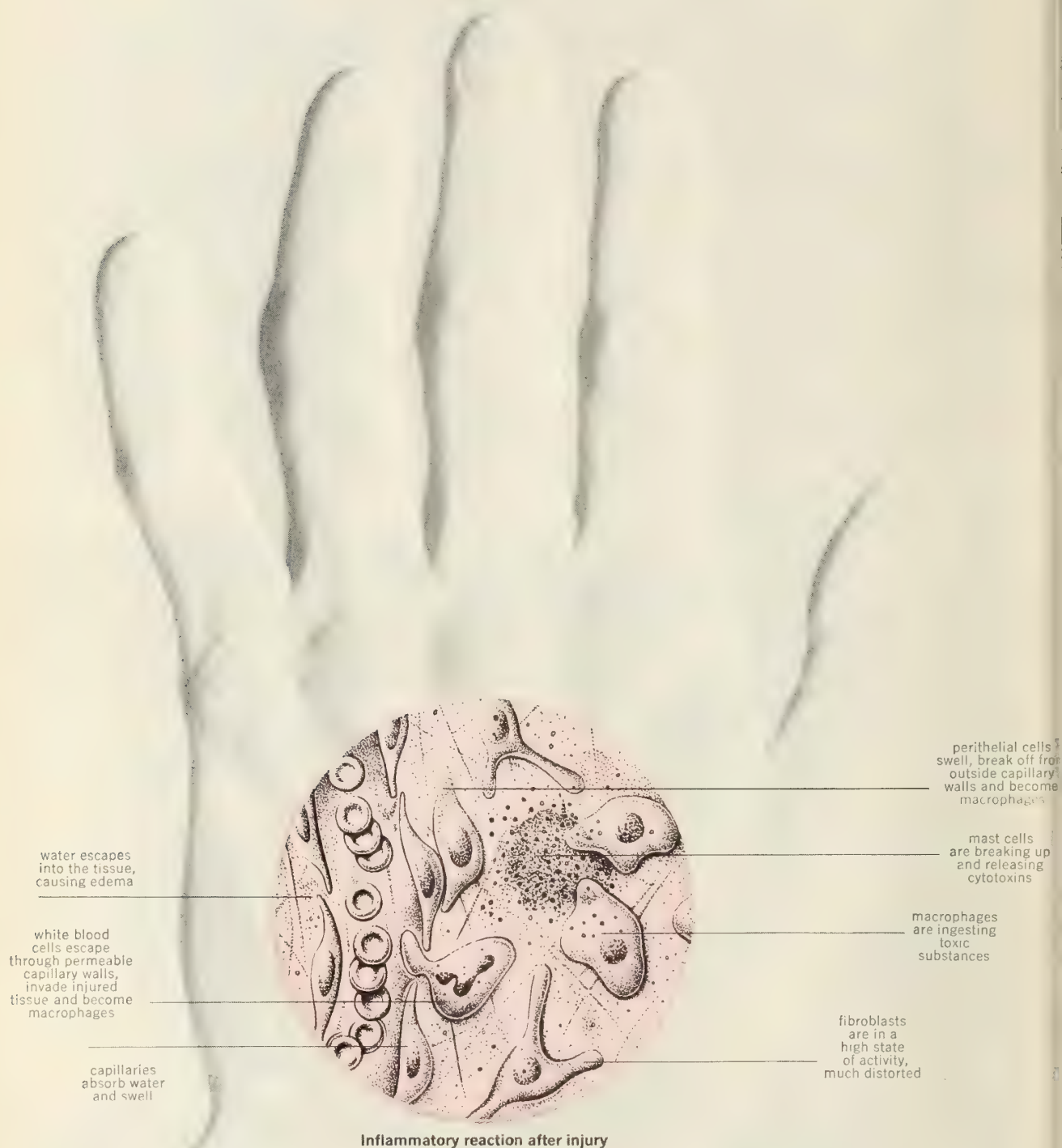
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**References:** 1. Kanee, B.: Canad Med Ass J 88:999 (May 18) 1963. 2. Scholtz, J. R.: Calif Med 95:224 (Oct.) 1961. 3. Jansen, G. T., Dillaha, C. J., and Honeycutt, W. M.: Arch Derm 92:283 (Sept.) 1965.

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Connecticut State  
Medical Journal

Volume 30 / October, 1966 / Number 10

## REM SLEEP / NREM SLEEP RELATIONSHIP THROUGHOUT HUMAN LIFE

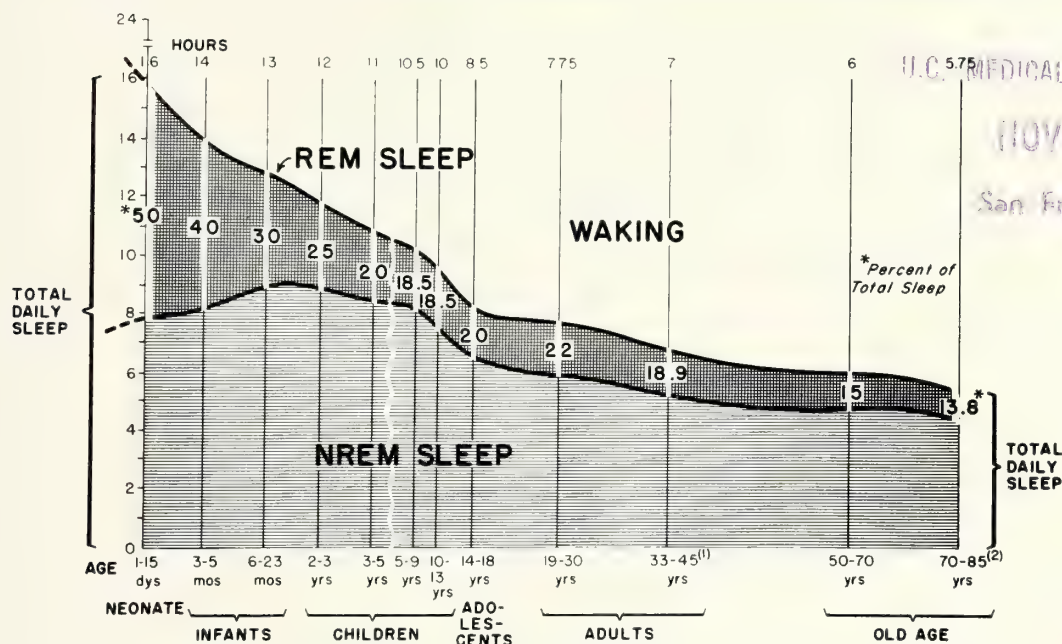


Figure 1—"Rem Sleep/Nrem Sleep Relationship Throughout Human Life,"  
Roffwarg, Howard P., *Science*, Vol. 152, pg. 607, April 29, 1966.

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## editorials

### The Nervous System And The Electrocardiogram

Our knowledge of the influence of the nervous system upon the heart falls roughly into three phases. The first was the recognition that heart rate and heart force could be reduced by action of the vagus and increased by action of the sympathetics. In the second phase of the development of our knowledge it was demonstrated by Nahum and his associates,<sup>1</sup> that cardiac arrhythmias are also closely involved with the action of the autonomic system upon the heart. In appropriate conditions the vagus contributes to the development of atrial flutter and fibrillation. On the other hand the sympathetics were shown to be intimately involved in the development of atrial tachycardia, ventricular premature systoles, and ventricular tachycardias.<sup>1,2</sup>

In the present phase, it has become evident not merely that disturbances of rate and rhythm are related to autonomic nervous system activity, but also that the ST segment and the T wave can be altered by action of the nervous system. There are reported numerous clinical observations in patients who suffer from central nervous system disease, of striking changes in the form of the T wave even though the heart itself is not damaged in any way.<sup>3</sup>

Normally the T wave is positive across the precordium especially on the left side because the apical and diaphragmatic heart surfaces repolarize

faster than the remaining surfaces of the ventricular myocardium. One reason for this is that the apex and diaphragmatic regions operate at a somewhat higher temperature than the rest of the myocardium. One reason for this is presumed to be that it rests upon the liver which is the hottest organ in the body.

When the repolarization of the apex is delayed by cooling with a thermal chamber placed over it, then the T wave promptly becomes inverted. When this region is heated then the T wave turns upright and may become much taller. The conclusion Nahum and his associates arrived at was that the form of the T wave is due to the interaction between apical and basal repolarization processes and that normally the positive T wave is due to more rapid repolarization at the apex and inferior regions of the heart.

With this as a background it is possible to form a hypothesis as to why the T wave form changes during nervous system disease. If the sympathetics altered the sequence of recovery from excitation by changing the duration of ventricular recovery in different regions of the myocardium then ST-changes could arise that are comparable with those described in the clinical situation of central nervous system disease. From certain patients with central nervous disease characteristic electrocardiogram disturbances have been described in which there is a prolonged QT interval and large inverted T waves but no other evidence of cardiac disease. A picture

### THE COVER

Figure 1. Graph showing changes (with age) in total amounts of daily sleep, daily REM sleep, and in percentage of REM sleep. Note sharp diminution of REM sleep in the early years. REM sleep falls from 8 hours at birth to less than 1 hour in old age. The amount of NREM sleep throughout life remains more constant, falling from 8 hours to 5 hours. In contrast to the steep decline of REM sleep, the quantity of NREM sleep is undiminished for many years. Although total daily REM sleep falls steadily during life, the percentage rises slightly in adolescence and early adulthood. This rise does not reflect an increase in amount; it is due to the fact that REM sleep does not diminish as quickly as total sleep. Work in progress in several laboratories indicates that the percentage of REM sleep in the 50- to 85-year group may be somewhat higher than represented here. Data for the 33- to 45- and 70- to 85-year groups are taken from Strauch (139) and Lairy (140) respectively.

comparable to that which occurs when the apex is cooled.

Janowitz, et al.<sup>4</sup> attempted to clarify the mechanism of this type of change in the electrocardiogram by stimulating either the right stellate ganglion and ablating the left or by ablating the right stellate and stimulating the left accelerator nerve. It appears from their studies that the right stellate ganglion innervates the anterior surface whereas the left stellate ganglion fibers innervate primarily the posterior ventricular surface. When the right stellate was stimulated recovery was accelerated in the anterior surface. Similarly a shorter recovery process occurred in the posterior ventricle when the left stellate was stimulated. Whatever changes in the T wave form that takes place appears to be the result of alterations in the recovery processes in these two areas caused by the sympathetic nervous system.

It is significant that the sympathetics do affect the rate of recovery in different parts of the ventricles as judged by changes in the duration of the refractory period. It is also revealing that the T wave form changes observed following unilateral alteration of sympathetic tone paralleled those electrocardiographic abnormalities seen in patients with lesions of the central nervous system. We have here an explanation of the clinical findings in such patients namely that the sympathetics in addition to altering heart rate, heart force, heart rhythm, also can alter the refractory period in different areas of the ventricle and produce significant T wave form changes which are on a functional basis.

This work of Janowitz, et al. amply confirms the explanation of the nature of the T wave offered by Nahum and his associates. It confirms the view that striking changes in the T wave form can arise not only from myocardial disease but also from functional changes caused by the action of the sympathetics on the heart.

L.H.N.

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## The Prevention Of Strokes

Strokes, it is well known, can be caused by emboli, or follow transient ischemic attacks or result from hypertension. Once a stroke is completed, it causes

some degree of brain damage, leaves the patient with less or more disability and must be regarded as a major set-back in the patient's life. Since we can do something in each of these three areas, the physician must give high priority to the prevention of a completed stroke. What can we do in each of the three areas mentioned above?

We know that in unselected cases of completed strokes emboli arising in such conditions as atrial fibrillation, myocardial infarction, cardiomyopathy or endocardial fibrosis, 5-10 per cent of them are caused by emboli. Furthermore, in acute myocardial infarction over 75 per cent of emboli go to the brain. Furthermore as many as 12 per cent of patients of unrecognized mitral stenosis first present themselves to the physician because of cerebral embolism.<sup>1</sup> In the last group of course prevention of embolism is clearly impossible, except perhaps by routine examination of people in positive health. Yet even after the first embolus there is still scope for prophylaxis against a second embolus which is likely to occur in 60 per cent of the surviving patients.

Regardless of what position one takes on the question of anticoagulant therapy in the management of cerebrovascular disease (in which there is some disagreement),<sup>2</sup> there is practically universal acceptance of its value in preventing cerebral embolization. Ideally of course such treatment should begin before the first embolism occurs, hence the necessity for beginning anticoagulant therapy in all cases in which a potential source of emboli is known to be present. The importance of this was shown by a series of 105 pts, with mitral stenosis whose symptoms were trivial or absent. Over a period of four and one-half years, 15 patients experienced a cerebral embolus, five of which proved to be fatal. What we do not know is what would happen in a similar series who were placed on anticoagulants from the standpoint of incidence of embolization or complications of the treatment itself, since continuing successful anticoagulation over a period of four and one-half years is no easy task. Of course if embolization has already occurred, the question still remains when anticoagulation should be begun, for fear of causing hemorrhage in the infarcted region of the brain. Marshall<sup>3</sup> believes it should be started immediately with heparin and then the coumarins. Some neurologists prefer to wait until danger of cerebral hemorrhage in the area of the acute infarct has passed.

The short-lived disturbances of transient ischemic attacks (TIA's) frequently give warning that a completed stroke is impending. It appears that this danger is much greater when the TIA's are occurring in the distribution of the carotid artery and its branches than when the vertebro-basilar system



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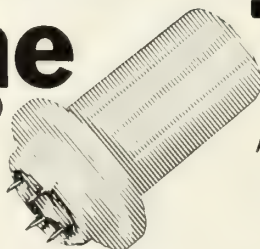
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is involved.<sup>3</sup> The appearance of TIA's in the carotid territory is therefore a signal for immediate action for if one should wait half of these patients may be expected to complete the stroke within a month.

There are a variety of causes of TIA and it is mandatory upon us to ascertain the immediate cause. Anemia or polycythemia can easily be recognized by a hematologic examination and overcome. Transient falls in arterial pressure such as may be caused by reduced cardiac output in severe hemorrhage acute myocardial infarction or shock can be combatted. Similarly hypotensive drugs poorly controlled can produce hypotension and produce a TIA. Finally transient hypertensive crises may also occur and give rise to focal neurological symptoms and signs instead of the more generalized disturbances of cerebral function usually associated with hypertensive encephalopathy. Parnate and cheese have been associated in the production of hypertensive crises. Patients with malignant hypertension who show evidence of being on the verge of developing it also require immediate control of blood pressure. The conditions mentioned above are readily detected and readily managed at the first examination but account only for a minority of the TIA's.

The majority of the TIA's require a careful assessment of the neck vessels. There may be a clue in the history as to what is likely to be found. For example, a past history of pain in a cervical root and a story that the TIA's tend to occur whenever the patient turns his neck suggests intermittent compression of the vertebral artery by osteophytes due to cervical spondylosis.<sup>4</sup> The association of attacks in the vertebrobasilar territory with the use of the upper limb and the finding of a difference in the level of blood pressure in the two arms raises the question of subclavian obstruction and blood diversion from the vertebral into the axillary artery.<sup>5</sup> The presence of a murmur over the bifurcation of the carotid artery in the neck indicates that a stenosis is probably present.

Obviously a necessary step toward rational treatment requires angiographic study in the stenotic and compressive lesions of the carotid subclavian or vertebrobasilar arteries. Then operations such as endarterectomy or the removal of osteophytes or restriction of neck movements through use of a collar must be evaluated in terms of the pathology thus uncovered. Alternatively one must consider anticoagulation therapy, since there is clinical evidence from controlled trials of the value of such therapy in some cases of TIA's.

There are of course certain theoretical difficulties in such an approach. The first is that platelet adhesiveness which leads to the formation of the first nidus of an arterial thrombus is not responsive to anticoagulation. The second is that the rupture

of an atherosclerotic plaque liberating cholesterol debris emboli which subsequently impact in the cerebral or retinal vessels cannot be prevented by anticoagulation. However such open wounds could form the basis for a fibrin-platelet clot which might be prevented by anticoagulation. In these instances the length of time necessary for epithelialization is not known but it has been suggested that such therapy be continued for at least a year.<sup>6,7</sup>

There is a third way to forestall the development of a completed stroke, namely by the proper management of hypertension. Cerebrovascular accidents are a common cause of death in patients with untreated hypertension. Even when a patient has already experienced a stroke, reducing the blood pressure can reduce the incidence of a recurrence and contribute importantly to lowering mortality. There are of course certain self-evident points that must be observed when employing hypotensive drugs in patients with cerebrovascular disease. Too great a reduction should not be sought and a diastolic pressure of 100 mm Hg is an acceptable level for the cerebrovascular patient.<sup>1</sup> Drugs which have a marked postural hypotensive effect should be avoided and the patient must be carefully instructed about the advisability of taking some gentle exercise on the bed before first arising in the morning. He must be told about the need to lower the head immediately if ever he should experience hypotensive symptoms.

Our knowledge of the basic causes of degenerative disease is as yet fragmentary and much work remains to be done on the pathogenesis of atherosclerosis before we can hope to prevent those vascular changes which are ultimately responsible for the completed stroke. Nevertheless we already have some means by which we can reduce the incidence of its most devastating effects on brain and the useful applications of those means discussed above should prove rewarding in the prevention of a completed stroke.

L.H.N.

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## Judging The Severity Of Heart Disease: The Clinical Use Of The Ballistocardiogram (BCG)

The BCG differs greatly from the ECG for the latter bears no quantitative relation to any aspects of myocardial performance whereas the BCG bears a very close relation to the dynamics of the circulation. After challenging a heart by a stress, it is possible to detect the less fit among healthy persons seeking employment as airplane pilots.<sup>1</sup> The BCG becomes abnormal in all or many patients after age 50. After a heavy meal an anginal patient will not show increased amplitude in the BCG. Smoking by a coronary patient causes deterioration in the force BCG. Smoking one cigarette by diabetics under 36 produces an abnormal BCG in over half. The physiology of this abnormal reaction is not worked out. Klensch<sup>2</sup> thought nicotine increased the cardiac load due to release of catecholamines. However carbon monoxide hemoglobin may also play a role.

If smoking produces such an effect on abnormal hearts, then other drugs may also do this. Profound BCG abnormalities are regularly caused by large doses of quinidine and vasopressin in experimental animals. When an anginal attack is terminated by nitroglycerin it is accompanied by great improvement in the BCG. It frequently does this when given between attacks. Still more unexpected is the marked improvement after nitroglycerin in the abnormal BCG of certain elderly persons who have never had angina pectoris or myocardial infarction.<sup>1</sup>

From the standpoint of prognosis the BCG is most helpful. Starr points out that diminution of the force BCG grows with age and if a patient already shows a small record, his chance of developing heart disease is increased and the mortality among such patients is also greater. In fact the more abnormal the form, the shorter is the average life duration. This is as true in patients not diagnosed as having heart disease as it is in those that were so diagnosed. Those patients with angina and with an abnormal BCG suffered three times as many infarctions as did those with a normal BCG.

In short, when one measures the various ways of judging the severity of cardiac involvement, the BCG is not inferior to other evidences (heart size, arterial pressure, ECG conduction defects) and has better prognostic value. The BCG therefore fully deserves to take its place beside the other valid

clinical methods in any judgment of the severity of heart disease. It can supplement the etiological and anatomical data and increase the accuracy of our estimate of the severity of any case and indicate the need for and direction which treatment should take.

Starr emphasizes his experience that over one-half of the cases of cardiac abnormalities encountered in the clinic will be missed without the force BCG record. So the question arises how best can the evidence of physiological cardiac abnormality be secured. Starr thinks that by simultaneously recording the BCG and the carotid pulse, it is possible to obtain greater insight into the two chief aspects of the heart's accomplishment: setting the blood in motion and raising the pressure throughout the cardiac cycle.

Once the two records are obtained, the quantitative analysis of cardiac function in terms of Newtonian physics becomes possible. A study of the behavior of both records immediately after the onset of ejection gives evidence of cardiac strength as it indicates the initial jerk of the cardiac contraction. If the person is healthy, the BCG is strongly deflected at this time and so is the initial deflection of the carotid pulse equally sharp and abrupt. If the initial deflections are less clearly marked, if the angles are rounded, if the slopes are less steep, if the onset of ejection becomes hard to find, then we have evidence of a heart beating weakly.

The amplitude of the initial deflection of the two records is another indication of cardiac strength. If the heart's contraction is jerky and incoordinate this is easily identified by abnormalities in the contour of the BCG. If the BCG and carotid pulse wave are similarly affected then an abnormality plainly resides in the left ventricle. Whereas an abnormal BCG not present in the pulse curve indicates a right ventricular abnormality.

There appear many diagnostic possibilities other than these. When the heart contracts, its energy is divided between energy of pressure and energy of blood flow. The relative proportions of these two kinds of energy differ widely from case to case and how best to combine the data given in the pulse curve and the BCG to obtain a single overall estimate of cardiac energetics is not yet at hand but presents some fascinating problems for further investigation.

Diagnosis however is not enough; we must also aim in the prevention and cure of diseases. The physiologic abnormalities detected by the BCG studies of the higher dynamic function of the heart must lead to knowledge of how to treat them better than we do now. The BCG can help us to decide which patients are being benefited by digitalis and those that may be injured by it. The BCG has



taught us that just as the action of nitrites given during an anginal attack is spectacular, it can also, when given in between attacks cause temporarily a marked improvement in the strength and coordination of the heart's beating and the same beneficial effect is seen in many elderly persons who have never had angina. Here is a case in which the therapeutic possibilities of the nitrites are better realized since BCG studies.

Abdominal binders are coming back into their own as a result of BCG studies in certain subjects. Binders were advocated in the past in the treatment of angina pectoris but have been little used in recent years. Starr reports a surprisingly beneficial effect on the BCG in patients with angina pectoris and this suggests that if a patient's BCG improves after applying a binder, that some cardiac difficulty in such patients may come from inadequate filling. This also points up the importance of abdominal exercises in such patients to strengthen the abdominal wall.

Starr points out that marked deterioration of cardiac function takes place after heart operations. He urges that knowledge of the preoperative myocardial state as determined by the BCG might help the surgeon to determine how to reduce damaging procedures during operation and help him to distinguish more from less harmful techniques. It might also help the cardiac surgeon if he had knowledge of the preoperative myocardial state to avoid the greater risks and thereby lower immediate postoperative mortality.

The BCG records can also be used to detect harmful situations. We all know that exercise makes the BCG of some patients better, but those of others worse, and so it follows that BCG monitoring should help us to detect which patients should exercise and how much should be undertaken, especially during convalescence from myocardial infarction. This type of monitoring with the ECG has been tried in post-myocardial infarction rehabilitation by graded exercise. However the BCG seems to be a better instrument to detect improvement in myocardial function than is the ECG. Furthermore we know that training improves the strength and coordination of peripheral muscles. Why should we not use the BCG to find out whether this is also true of the heart muscle.

Many problems about myocardial function will now be studied and solved which we have not been able to settle by history, physical findings, X-ray and ECG. With the BCG we will obtain a direct measurement of myocardial function and learn how well the heart is raising the pressure and setting the blood in motion as it pumps it about the body.

L.H.N.

## Metabolic Obesity And Genetics

Realizing that hunger and satiety are regulated by centers in the hypothalamus, then a regulatory type of obesity would be one in which the centers are damaged. These would be exemplified by obesities induced by destruction in the ventromedial nuclei bilaterally. Such destruction could be achieved surgically. It has also been produced by Mayer after administration of gold thioglucose. This latter substance seems to be taken up selectively in the ventromedial nuclei and the gold destroys the neurons in this area.

Whatever method is used to injure the ventromedial nuclei, the resulting syndrome in mice is one of hyperphagia and obesity to four times the normal weights. Their rates of lipogenesis and cholesterologenesis (as measured by incorporation of radioacetate into hepatic and extrahepatic fatty acid and cholesterol *in vivo* and *in vitro*) increases in proportion to the amount these animals are allowed to overeat. One can make such animals return to normal in every way by fasting.

Metabolic obesity is different. In this type the primary lesion is an inborn or acquired error in the metabolism of tissues *per se*. In this type, peripheral metabolic dysfunction may in turn interfere with the proper function of the nervous system. One example of metabolic obesity is found in mice and termed hereditary obese hyperglycemic syndrome. It can produce as extreme an obesity as the hypothalamic types but their hyperphagia is less pronounced and relative inactivity is partially responsible for their caloric surplus.

The adipose tissue of these animals also has abnormal characteristics such as lipogenesis even in fasting and decreased glucose uptake. There are no effects of epinephrine on fat mobilization and fatty acid release from adipose tissue. There are also some pancreatic changes as well, for glucose accumulates in the blood and the pancreas becomes exhausted because of resultant increased production of insulin.

Mice made obese by grafting ACTH secreting tumors also show a large number of metabolic abnormalities. The blood glucose levels are high and show remarkable stability under fasting conditions. Furthermore, the fasting condition does not reduce liver glycogen levels and the rate of lipogenesis during fasting is higher than normal. Even more remarkable is that during starvation such animals develop no ketosis.

The question thus arises whether similar distinctions between regulatory and metabolic obesity may also occur in man. Since they occur in animals, they should also be found in man and a search is under way to see if they do. All of this leads to the question of the role of genetic factors in either type of obesity. In laboratory animals genetic factors are

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**\* Reference:** Litchfield, H. R.: Archives of Pediatrics,  
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clear cut. There is the hereditary obese hyperglycemic syndrome mentioned above and yellow obesity, a dominant syndrome of mice heterozygous for this gene. Quite different is the New Zealand obesity, a recessive syndrome of obesity and diabetes in mice. Then there is a genetically controlled spontaneous degeneration of the ventromedial area of the hypothalamus. There are many others described in laboratory and farm animals.

With such well established evidence of the relation between obesity and genetics in animals one would expect that in man also genetics may play a role in metabolic obesity and other forms. However to demonstrate a hereditary nature of familial obesity in man is much more difficult. We know it runs in families. Bauer<sup>2</sup> in a series of 1,000 obese patients found one or both parents were obese in 73 per cent. This finding has been repeatedly confirmed by many others. Mayer in Boston also found a high degree of correlation between overweight in parents and children. On the other hand only nine per cent of children of average weight parents were found obese by Gurney.<sup>3</sup>

It is not easy to interpret this kind of data without considering interaction of cultural background with genetics to determine the incidence of overweight. There are conflicting views on relation of ethnic origin and severity of obesity. The possible interaction of environmental and genetic factors is hard to separate. Some of the most useful tools of genetics for example, parent to offspring, brother to sister, mating, are not applicable to human studies. This leaves study of genetic factors in human obesity to study of twins, study of sex ratios, and study of somatotypes in relation to obesity.

The method of studying the problem in twins is simple. Characteristics of obesity should occur in identical twins (monozygotic) but should not necessarily appear in fraternal twin pairs. The weight in identical twin pairs was found pretty constant by Mayer and thus suggests that genetic factors are of paramount importance.

Striking indication of genetic determination in human obesity comes from evidence from sex ratios in children. There is as Mayer states relative excess of fat females, over fat males, among parents and siblings of the obese (60 per cent are fat females and 40 per cent are fat males). In adopted children there was no correlation between them and parents whereas there was a correlation between natural children and their parents. Where food is abundant and hard physical labor unnecessary, it could very well be that genetic factors could dictate predisposition to overweight. What the mechanism of heredity may be is still missing.

The final point that Mayer makes is that there is a correlation between the patients somatotype

and obesity. Obese girls differed from non-obese in two particulars; the amount of fatty tissue, and their somatotype. The obese adolescent girls appeared to be more endomorphic and considerably less ectomorphic than the non-obese girls in the general population. The obese group had large skeletons and muscle mass in spite of inactivity. They also showed an absence of narrow elongated extremities. Seltzer and Mayer<sup>4</sup> found very few girls with long tapered fingers who are obese. In adults, however, the problem is more complex.

If there is a close correlation between obesity and body types in adolescents this obviously argues for the genetic determination of obesity because the hereditary character of the determination of body build has been repeatedly demonstrated.<sup>4,5</sup>

L.H.N.

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## Cardiac Lymphatics And Their Relation To Cardiac Function

Only a few of the tissues of the body do not have lymphatic channels. Those include portions of the skin, the central nervous system, deeper portions of the peripheral nerves, the endomysium of the muscles and the bones. However, even in these structures are minute passages through which extracellular fluid can flow and eventually this fluid flows to other areas that do have lymphatic channels or that can empty directly back into the blood.<sup>1</sup> But in all other tissues the lymphatic system is highly developed and represents an accessory route by which fluids from the interstitial spaces can flow back into the blood. Most important is the fact that lymphatics can carry proteins and even large particulate matter away from the tissue spaces, neither of which can be removed by absorption directly from the blood capillary.

The concentration of protein in the lymph from most areas of the body is about 1.5 grams per cent which is also the concentration of the interstitial fluid. To be sure some lymphatic drainage as from the liver and gastro-intestinal tract contain protein concentrations as high as 3-5 per cent. This removal of protein by the lymphatics is an absolutely essen-



## Breast-feeding and the “modern mother”

Despite a mild resurgence of interest in the importance of breast-feeding a few years ago, many women today do not choose to nurse their young. This is for a variety of reasons—social, economic, cultural and sometimes medical. In such cases the physician's task is to find the most suitable means of preventing lactation and easing the pain of breast engorgement.

### The means of therapy

The value of hormone therapy for this indication is of course well established. Both androgen and estrogen are known to inhibit the production and secretion of the lactogenic hormone by the anterior pituitary. As estrogen levels decline sharply at parturition, lactogenesis is established. When androgen and estrogen are administered to the patient before the release of the lactogenic hormone lactation and breast engorgement are usually prevented.

### The time of therapy

The time of administration of this combined medication is crucial; it must be given early enough to suppress the pituitary prolactin and last long enough to permit physiologic readjustment during the puerperium. Excellent results are most often seen when therapy is administered before the onset of the second stage of labor.

However, factors other than effectiveness must also be considered. The agent selected should not interfere in any way with parturition, subsequent uterine involution and the restoration of normal ovarian cyclic function. Furthermore, it should not cause rebound breast engorgement or other manifestations of hormonal imbalance.

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### Dosage:

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### Contraindications:

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### Precautions and Side Effects:

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tial function without which the cells would die probably within 24 hours. The reason for this is that only a small proportion of the proteins that leak into the tissue spaces from the arterial capillary can diffuse back into the capillary because there are five times as many proteins in the plasma as in the interstitial fluid. As the fluid is reabsorbed at the venous end of the capillary, most of the protein is left behind and tends to accumulate in the interstitial spaces. This in turn increases the tissue colloid osmotic pressure and further decreases reabsorption of fluid by the capillaries.

It can be seen that unless the protein in the interstitial fluid is carried away by the lymphatics, exchange between plasma and interstitial fluid would cease and cells would be choked off from receiving nutriment and excreting waste products. Therefore it is valuable that the quantity of interstitial fluid be maintained at a minimum by the lymphatic channels so that rapid transfer of these substances can occur. When extracellular fluid edema develops the distances that nutriment and excreta must travel increases markedly and nutrition of the cells may suffer greatly.

Usually the flow of lymph from any tissue is relatively small compared to tissue irrigation caused by exchange of fluid between the plasma and the interstitial fluid. However, when elevated capillary pressure develops as in heart failure or decreased plasma colloid osmotic pressure, then amount of interstitial fluid increases until edema develops. If increased permeability of the capillaries increases as during infection or anoxia, then also extracellular fluid volume increases and the tissue pressure will rise. If the lymphatic channels remain open the rate of lymph flow in such instances may rise to as much as 10 times the normal. If the lymphatic drainage from any area of the body becomes blocked, more and more protein collects in the local tissue spaces until finally the concentration of this protein may approach the concentration of protein in the plasma with the resulting dire consequences mentioned above.

Such lymph obstructions are known to follow filariasis and also following operations for removal of cancer because adjacent lymph nodes must be removed also. It also follows inflammations in certain tissues leading to dire consequences depending upon the degree of lymphatic involvement. Inflammatory edema occurs for a variety of reasons. One is damage to the cell itself which causes autolysis of organic substances inside the cell. The sodium pump of the cell membrane becomes inoperative causing large amounts of Na to collect inside the cell. This raises the osmotic pressure in the cell greatly and causes their swelling. Such damaged cells can release toxic substances into the

surrounding interstitial fluid and some will attack the local capillaries and make them more permeable. Others will cause the proteins that diffuse into the lymphatics to coagulate. In this way there occurs increased capillary permeability together with lymphatic blockage.

Such general principles should be borne in mind in regard to the function of any organ, and the heart is no exception although we rarely think of circulation through the coronary system, except in terms of its arterial structure. The fact is that the heart has a rich lymphatic system, richer in youth and young animals and less so in middle-aged and elderly persons. Johnson and Blake<sup>2</sup> have presented evidence about this system in humans, dogs and pigs using an old method of topical application of hydrogen peroxide as well as injection techniques.

In general all three species have extensive sub-epicardial and subendocardial networks with collecting channels directed towards large ducts in the AV sulcus, continuous with the main cardiac lymph duct. In young animals, the dog and pig, the subendocardial systems communicate via transmyocardial channels and channels in the supporting structures of the AV valves. In humans these communications have not been identified with certainty. Lymphatics are seen in both AV valves of animals but thus far have been seen only in the mitral valves of humans. Since lymphatic channels are necessary for the maintenance of the integrity of cells, we have reason to believe they exist in the heart even though they have not yet been identified in every part of it. If areas in the heart have thus far not revealed lymphatic channels it may be due to inadequacy of the method of visualization or decline in lymphatic channels with advancing age or as a result of disease.

It is time then that we began to think of the possibility that alterations of cardiac lymphatic drainage may have clinical significance. The coarseness of lymphatic plexuses and the larger diameter of the individual lymphatic capillaries in the human subendocardium compared to young animals may be a reflection of impairment of lymph flow. This could result from fibrosis and thickening of some areas of the heart framework, especially the annuli fibrosis which has been reported to occur. The result of partial or complete lymph obstruction at this level will be evident in nearly all areas of the heart including the valves.<sup>3</sup>

According to Gross<sup>4</sup> the mitral valve ring may be affected early in rheumatic fever with subsequent involvement of aortic and tricuspid valves by continuous spread along the fibrous framework which has elements in common with all three valves. Now that we know lymphatics exist, perhaps this is the means whereby the rheumatic process spreads.

Inflammatory reaction with subsequent granulation and fibrosis of the annulus could produce impairment of lymph drainage of the AV valves and make them susceptible to infection, inflammation and fibrosis. A mechanism of this sort may help explain thickening and the frequency of bacterial endocarditis in patients with rheumatic valvulitis, especially of the mitral valve and of aortic endocarditis in the aged.

Then there arises the question of what happens following replacement of diseased valves by valve prostheses. Mechanical obstruction of lymphatics in the valve rings and the AV sulcus may be a factor having influence on the success or failure of these devices and other cardiac function during the post-operative period.

Disturbances of subepicardial lymphatic flow may be significant in the development of post-pericardiotomy syndromes and on production of pericardial effusion. Inflammatory diseases of the myocardium must certainly cause some lymphatic obstruction and be a factor in reduced myocardial efficiency in case the patient recovers.

The studies on cardiac lymphatics bring into focus a wide variety of cardiac disorders that may arise not from disorders of the coronary circulation but from the disturbances of the lymphatic system in the heart.

L.H.N.

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## Membrane Transport Of Sodium (Na) And Potassium (K)

Membrane transport of Na and K subserves a wide range of cellular functions. The ions play a vital role in excitation and conduction in the three kinds of muscle cells and also in the central nervous system where they are also involved in transmission over synapses and the production of generator potentials in sensory endings. Secretory processes both in the gastrointestinal tract and kidney are dependent upon Na and K transport. In growth and development these ions play a role in regulation of cell volume and of protein synthesis. Hormones such as vasopressin and aldosterone exert an important effect upon movement of these ions. Recently secretion of insulin has been found

defective whenever the K ion concentration is too low in the extracellular fluid. All of these and many more aspects of physiology and medicine are intimately related to the transport of Na and K across cell membranes. It is entirely appropriate therefore that we should attempt to understand more clearly the mechanisms of these processes.<sup>1</sup>

The concentration of Na ion outside the cell averages 144 meq. and inside only 10 meq. The concentration of K ion lies in the opposite direction with 141 meq. inside and 4.5 meq. outside. These differences are maintained by the continuous transport of sodium to the exterior and K to the interior except during depolarization. The leak of Na ion inward and of K outward from the cell is driven by the differences in electrochemical potential of the transported ions in the phases bathing the two sides of the membrane, i.e. cytoplasm and extracellular fluid. This kind of transport is sometimes termed passive or dissipative.

The transport of Na ion to the exterior against a gradient is so important in cellular function that it is commonly called the sodium pump and plays an extremely important role in the normal physiological processes noted above and especially in depolarization and conduction of excitable tissues such as muscle and nerve. These active transport processes are driven by forces generated within the membrane itself. It is these forces which maintain the inequities of ion concentration on each side of the membrane. The energy for these processes derives from chemical reactions occurring within the membrane.

The question of course is why is it that cell membranes act selectively on Na and K transport. This involves understanding the nature of membrane structure and function. There are known specific compounds which modify the selectivity of a biological membrane for K and Na. For example, tetrodotoxin, a poison produced by the Japanese puffer fish, prevents the increase in Na permeability which is associated with the action potential of skeletal muscle and squid axon. In this way it prevents development of transport pathways which are briefly required for depolarization. In a similar way increase in permeability of r.b.c. membrane to K can be experimentally induced by metabolic and oxidative changes in the cell.

There is good evidence to indicate that the Na pump derives its energy from hydrolysis of ATP although Hoffman and Kregenow<sup>2</sup> believe there must be other sources for the energy of the sodium pump besides ATP.

In a number of tissues active transport of amino acids and sugars are intimately associated with Na transport. For example, the rat diaphragm needs sodium to take up glycine. In fact the elucidation of the mechanisms of the interaction between Na





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and K transport of sugars and aminoacids is an important question for investigation.<sup>1</sup>

Then there is the question of how hormones such as vasopressin modify the transport of Na and K across membranes. As far as aldosterone is concerned Edelman<sup>3</sup> believes that Na transport in the toad bladder is induced by the synthesis of a protein because actinomycin which prevents protein synthesis, blocks Na transport. How does all this happen?

In the membrane there is found an enzyme activity Na and K stimulated ATPase (S-ATPase). This enzymatic activity is extremely widely distributed in many different types of cells. In r.b.c. Na and K activities this enzyme whereas cardiac glycosides inhibit it. This closely parallels the dependence of active K-Na transport on these factors. A study of these problems is extremely difficult but it must be solved.

Structurally S-ATPase seems to be a lipoprotein which requires the presence of lipid for optimal activity. Two aminoacids, cysteine and serine, seem somewhat involved in S-ATPase activity. Magnesium activates it by interacting directly with the protein. The mechanism by which Na and K modify activity is not yet clear. The study has been done by labelled ions which make it easy to detect minute quantities. Out of them have come a view that Na is necessary for the formation and K for the hydrolysis of a phosphorylated intermediate in the S-ATPase.

From now on it is crucial that we determine the size of the membrane regions which are involved in passive and active transport of Na and K. Another problem is to learn whether transport occurs in both directions in the membrane itself at different sites in it. As Tosteson points out, both theoretical and empirical considerations strongly suggest that pump and leak must be closely connected in order to control the cell composition of K and Na.

A third important area for future work involves how growth and differentiation of membrane occurs with respect to transport of Na and K. One would suppose that these processes are controlled genetically. For example, genetically controlled changes in the membrane of sheep r.b.c. vary in maturing but non-dividing erythrocytes as compared to mature r.b.c. as regards Na and K transport. How does DNA in the stem cell direct these changes in membrane function. Are the Na and K transport changes intrinsic to the differentiating r.b.c. or due to the effect of a hormone produced elsewhere in the body. Are the permeability changes due to alterations in the lipid or protein content of the membrane.

It seems remarkable that such fundamental properties of the living cell membrane involved in Na and K transport upon which life itself de-

pends should have so little known about them and so much yet to be explored. This is not to speak of transport of such other necessary substances that must cross the membrane such as aminoacids, glucose, lipids and hormones, also required for maintenance of the living machinery in the cell.

L.H.N.

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## Reflections On The Action Of Diuretics

The purpose of a diuretic is to reduce the volume of extra-cellular fluid to normal, that is to eliminate and prevent formation of edema. These ends are accomplished by excretion of an amount of salt greater than or equal to the intake. In actual practice it turns out that all useful diuretics produce their effects by interfering with the reabsorption of sodium (Na) from the distal tubule lumen and in some cases in the ascending limb of the loop of the Henle. There apparently is no inhibition to reabsorption in the proximal tubule by any of the present diuretics in use although this is the place for maximal reabsorption of Na. For us clinicians however it is not essential to know the site and even the mechanism or action of diuretics unless it may become a guide to pharmacologists in the development of new agents. Nevertheless, we do need to know something about the relationship of urine flow and urine composition combined with an appreciation of the potency of various diuretics since such knowledge will generally provide an adequate basis for their use.

Mercurials in a patient pretreated with acidifying salts may produce a diuresis of 15-20 per cent of the glomerular filtrate. Fortunately they are short-acting and the danger of producing hypokalemia and hyponatremia is minimal. However, if they were used regularly these complications could be readily produced. The thiazide group of drugs do not produce half of the diureses of a mercurial, but they are given steadily over a long period of time and so we do encounter potassium wastage and occasional hyponatremic states. The new diuretics about to be released, ethacrynic acid<sup>3</sup> and furosemide<sup>2</sup> can produce even a greater diuresis than the mercurials and doubtless will produce a higher incidence of hypopotassemia and hyponatremia unless



we are alert to these dangers and employ them intermittently as we now do the mercurials.

As far as we know all the useful diuretics produce their effects by interfering with the reabsorption of Na from the tubule lumen. At the same time it often happens that the chloride ion commonly exceeds that of Na and the deficit is made up by K and  $\text{NH}_3$ . In consequence since the introduction of thiazides eight years ago, the problem of K loss has become important. In individuals who are accumulating edema, there is a marked reduction of Na excretion and this retention is frequently accompanied by hypersecretion of aldosterone. In such patients a diuretic will cause more Na delivered for exchange and K secretion is markedly increased. In the heart failure patient with edema there is not much aldosterone secretion and the initial K loss from diuretics will be rather modest. But we administer a diuretic and a salt-free diet to such patient, at this stage, aldosterone secretion increases and K loss is enhanced.

As mentioned above the problem of K loss became common only with the introduction of the thiazide diuretics. Mercurial diuretics also produce K wastage but because they were used intermittently a considerable interval between injections permitted the patient to recover his K losses from the normal dietary intake. With thiazides, the patient is under the continuous effect of the diuretic and K loss accumulates unless it is supplemented. It follows that it would be more effective and easier to omit the administration of the diuretic a few days at a time to avoid the dangers of potassium wastage especially in cases already digitalized. This danger will become especially important because new drugs will be coming up with greater capacity to produce sodium depletion and hence stimulate aldosterone secretion. The continuous administration of such drugs after "dry weight" has been reached will almost certainly lead to potassium problems among others.

Another serious problem in the continuous use of powerful diuretics derives from the relation of water to salt losses. Normally the osmoreceptor—antidiuretic hormone—renal tubule system, maintains the osmotic pressure of the body within relatively narrow limits. A solute loss from the body would result in lowering of the osmotic pressure and immediately there is a loss in the urine of an equivalent volume of water, thus restoring the osmotic concentration to normal.

As long as the system regulating osmotic pressure is operating normally, salt loss through restricted salt intake or through loss in the urine will lead to equivalent losses of extracellular fluid volume. But there are edematous patients in whom the regulation of osmotic pressure is no longer effective

and hyponatremia develops and we must be on the lookout for this not uncommon instance.

In the development of hyponatremia two groups of patients are involved and they represent the two ends of the spectrum of responsiveness to diuretics. One is the group of highly resistant patients who suffer from advanced cardiac failure or cirrhosis who are markedly edematous and yet respond poorly to most measures including diuretics. They are hyponatremic because their disorder of electrolyte excretion has extended to involve a disorder of water excretion. This is a result of reduced glomerular filtration rate as well as increased secretion of antidiuretic hormone (ADH) not related to any normal stimulus for its production by the osmoreceptors. There develops a failure of regulation of osmotic pressure.

Such patients present a difficult problem in therapy. Giving them salt will only increase their edema. Measures to improve their circulatory status are important so that increased cardiac output will increase the glomerular filtration rate whose reduction is one of the causes of hyponatremia. Otherwise the only effective measure appears to be a rigid restriction of fluid intake, often resisted by the patient. Such a measure is only slowly effective at best since it ordinarily involves a negative water balance of only a few hundred m.l. a day in a patient who may have an excess of water of 5-10 liters. In the treatment of severe cardiac failure restriction of water intake would help to arrest dilution before it has become severe.

The other group of patients in whom hyponatremia develops are those who have responded too well to diuretics and have gone past the cure of edema to a depletion of their extracellular fluid volume. These have developed a borderline circulatory insufficiency with reduced glomerular filtration rate. Again there is an increased secretion of ADH for reasons unrelated to the demands of the osmoreceptors to maintain normal osmotic pressure.

The indicated treatment in this group is different from that in the first group of patients, for in these patients the administration of sufficient salt to restore a normal balance of extracellular fluid will permit the normal regulation of water excretion.

There are a few general principles which Berliner<sup>1</sup> offers that should be kept in mind by all practicing physicians. There appears to be little difference in action between any of the diuretics on potassium loss, on interference with urate excretion and carbohydrate utilization provided the dose is adequate to produce the maximum effect.

To avoid potassium loss he advises trying intermittent therapy whenever intensive therapy is not required. In the latter case adequate potassium supplements and high potassium containing food

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The following is a brief precautionary statement. Before prescribing, the physician should be familiar with the complete prescribing information in SK&F literature or *PDR*.

*Precautions:* Use with caution in patients hypersensitive to sympathomimetics or barbiturates and in coronary or cardiovascular disease or severe hypertension. Do not use in patients taking MAO inhibitors. Excessive use of the amphetamines by unstable individuals may result in a psychological dependence; in these instances, withdraw the medication. Use cautiously in pregnant patients, especially in the first trimester. *Side effects:* Insomnia, excitability and increased motor activity are infrequent and ordinarily mild.



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are required and these are not found in combinations of thiazide and potassium pills which actually give a false sense of security.

The chief value of aldosterone antagonists which by themselves are rather weakly diuretic is to combine them with more effective diuretics in reducing K losses and increasing Na loss in the more diuretic resistant patient. Here caution is urged to avoid an undesirable degree of potassium retention and hyperkalemia.

Ethacrynic acid<sup>5</sup> and furosemide<sup>4</sup> are likely to become available in the near future and have the advantage of being not only at least as potent as the mercurials in causing massive diuresis, but have the advantage over mercurials in that they are relatively non-toxic on oral administration and their efficiency does not depend on the acid-base status of the patient as does that of the mercurials. In consequence, they can be given in acute heart failure with pulmonary edema because they can produce massive diuresis within a few minutes of their administration by mouth.

The widespread use of such potent diuretics requires a note of caution. We still have little to gain in the vast majority of patients in whom diuresis is indicated by replacing the thiazides which are eminently satisfactory with new and more powerful diuretics. We probably should employ them only when the currently available therapy is inadequate because we still do not know their hazards. The tendency to switch to the newest and most potent agents available could in this area lead to a situation in which striking benefits to a few patients are more than outweighed by the unnecessary problems incurred in the many others who do very well with the thiazides. In short, discriminating selection of patients for the new diuretics to come will be a measure of our understanding of the disturbances involved in edema and the way diuretics act to relieve it as well as the untoward effects they can also produce.

L.H.N.

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Thyroid Nodules After Fallout

In 1954 the people on the island of Rongelap in the Marshall group saw in the early morning the blinding flash of a detonation of a United States nuclear device. With a shifting of the wind, a white snow-like fallout occurred throughout that day. These innocent victims of the cold war received the largest radiation; 175 rads of whole body gamma radiation, thousands of rads to the skin, largely beta, from deposit of fallout material on the body and significant amounts of radionuclides absorbed by radiation and consumption of contaminated food and water. It took three years for the radioactive levels to subside sufficiently before the evacuated people could return to their homes.<sup>1</sup>

There were extensive skin burns, some of which left deep scars on healing. Radioisotopes of strontium, barium, and iodides were absorbed in greatest amounts. The radiation proved to be sublethal, but the depressed hematopoietic system took eleven years before returning to normal. There was an apparent increase in miscarriages and still-births in the exposed women as compared with unexposed women over the four years after exposure and a few congenital abnormalities were also found in babies born to the exposed women. There was a slight retardation of growth in the boys exposed at 1-5 years of age, most marked in those exposed at 12-18 months of age.

Until 1963 no thyroid abnormalities were detected in exposed or in a comparative unexposed population, perhaps because these people tend to have an elevated serum PBI normally and a decline in thyroid activity to critical levels would take a longer time to register. This absence of abnormality was somewhat surprising because radioiodine entered the body through water and the total estimated dose to a child's gland was about 1,000 rads. The thyroid glands received additionally 175 rads from external gamma radiation. However, since 1963 eleven cases of thyroid nodules varying in size from 2-8 mm. were discovered and the highest incidence was in children exposed at less than 10 years of age and higher in females than males.

We needn't deal with the correctness of total thyroidectomy as a treatment in six of these cases, two of whom developed hypoparathyroidism as a complication of the operation. But it is important to emphasize that in this fallout of the cold war, a great burden fell on the children, just as Professor Jean Mayer pointed out in a letter to the New England Journal of Medicine that the American attempt to starve the resisting Vietnamese into submission places its greatest burden also on infants and children.

The radiation etiology of multiple thyroid nodules in Conard's patients appears to be reason-

ably certain. The thyroid glands received a substantial dose of radiation both from external sources and from radioiodines taken internally and the incidence of thyroid abnormalities was high in the exposed group and absent in an unexposed control population living in the same island group.

Adenomas and even cancer of the thyroid can be produced in laboratory animals by a variety of agents or regimens that interfere with the ability of the gland to synthesize thyroxine. Iodine deficiency thiourea, x-irradiation of the gland with  $I^{131}$  have all been shown to produce both benign and malignant neoplasms. Subtotal thyroidectomy in the rat has been reported to cause adenoma formation in the remaining tissue two years later. All of these procedures produce hypothyroidism of varying degree and this serves as an effective stimulant to the liberation of TSH by the pituitary gland. Under the influence of TSH the thyroid gland first undergoes diffuse hyperplasia and hypertrophy and finally adenomatous formation.

In the case of radiation damage besides the occurrence of a stimulus to cell growth from the resulting hypothyroidism and increased TSH secretion, there also results cell damage particularly to its genetic apparatus. This kind of treatment then produces cell mutation and cell growth at the same time, a potent combination in the promotion of carcinogenesis.<sup>2</sup>

The increased sensitivity of children's thyroid glands to the development of neoplastic changes from radiation exposure, have been amply demonstrated especially after irradiation of the thymic region in infancy and the later development of thyroid cancer.<sup>3</sup> Similarly the development of adenomatous lesions of the thyroid in children 5-11 years after treatment with  $I^{131}$  for thyrotoxicosis has also been reported.<sup>4</sup> This is not surprising because there are 3-4 cell divisions that occur as the infant gland grows from about 1.5 grams to a mature 17 grams.<sup>5</sup> If irradiation is administered to children's gland by whatever source, the growth principle combines with the genetic damage element to increase the hazard of cancer formation. The growth element would not be a factor in adult glands and such glands should not be so prone to carcinogenic effects of radiation.

Conard reminds us of the increased tendency of thyroid carcinoma in inhabitants of Hiroshima and Nagasaki who were exposed to radiation from the atomic bomb explosion. Recently it has been observed that a reactor accident in the West may have left its trail of thyroid nodules downwind. At the same time therapy with radioactive iodine for childhood thyrotoxicosis must be viewed with considerable reserve.

The therapeutic implications of  $I^{131}$  effects upon children and adults are quite clear. The first is

that rapid institution of potassium iodide therapy for suppression of thyroid uptake is indicated in any population exposed to fallout. The second is that thyroid treatment of patients with nodules of the thyroid gland will suppress liberation of TSH and reduce the incidence of  $I^{131}$  induced adenomas. A third is that people subjected to  $I^{131}$  absorption after atomic explosions will need medical supervision for life.

It is depressing to be reminded that American atomic tests "inadvertently" injured a significant number of innocent people. However, recording and analyzing these adverse effects may bring some good, if the alarm physicians feel about the serious consequences of atomic explosions also becomes a part of the thinking of those who support the cold war.

L.H.N.

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## The Microcirculation:

### 1. Functional Pathology

The microcirculation (M.C.) has been termed the "third force" in the cardio-vascular circuit, the heart and peripheral large vessels being the other two. The M.C. has lagged behind in our study of the circulation, at a time that spectacular advances have taken place in the study of intracardiac events and in cardiovascular surgery. Nevertheless if the M.C. fails, tissue nutrition becomes impaired and cardiovascular repair becomes futile.

One can look at the M.C. with a magnification of 2000-4000 in the retina, the conjunctiva or the nail fold in the skin, muscle, kidney, liver and many other organs. One of the obstacles to the study of the M.C. by the clinician has been the scarcity of the clinical tests permitting an evaluation of the morphology and function of the minute vessels. Of course in the skin one can test the capacity of the M.C. to dilate by producing a histamine flare as Sir Thomas Lewis did, or by the response of temperature and pulse wave to a nerve block.<sup>1</sup> In the acute M.C. failure that occurs in



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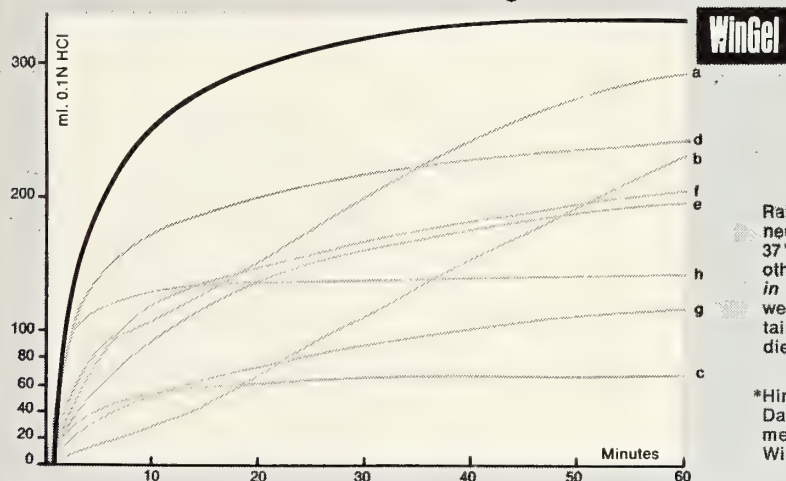
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\*Hinkel, E. T., Jr. (New York): Data in the files of the Department of Medical Research, Winthrop Laboratories.

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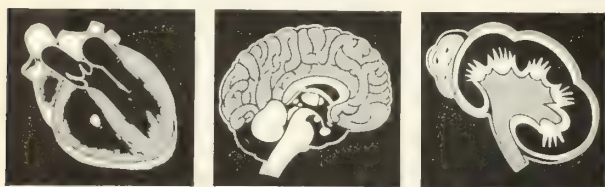
(10584)

# Behind continued high blood pressure readings lies the possibility of organic damage

1-13

**M**ANY OF THE aspects of essential hypertension are unpredictable—either because there are a number of mechanisms involved or because individuals differ in their responses to these mechanisms.<sup>1</sup>

There is one aspect of hypertension, however, that seems, in many cases, predictable. "... when the blood pressure is elevated to a marked degree for an adequate period of time, this in itself leads to perpetuation of the syndrome with resulting vascular damage throughout the body."<sup>14</sup> All too often the disease progresses until there is damage to one of three vital organs: the heart, the kidney, the brain.



"Hypertension is certainly a major factor in the genesis of coronary heart disease, and it is even more important when compounded with obesity."<sup>4</sup>

"[Vascular deterioration] can be clearly seen in the kidney with a degree of damage that can be measured by renal function studies."<sup>10</sup>

"... most evidence suggests that reduction of blood pressure, when it is too high, not only relieves the heart of excess work but reduces vascular damage."<sup>1</sup>

**"In short, treatment is indicated."**<sup>1</sup>

Antihypertensive therapy will not restore the blood vessels to normal. Yet many of the vascular changes and symptoms caused by increased blood pressure may be arrested or alleviated when the blood pressure is reduced to normotensive levels.<sup>7</sup>

Reducing the blood pressure helps curtail further vascular damage and improves the prognosis — when damage is not too far advanced before therapy is started.<sup>14</sup> Essential hypertension is an indication not only for treatment, but for early and adequate treatment of the patient in question.

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Rautrax-N combines the antihypertensive-tranquilizing action of whole root rauwolfia with the antihypertensive-diuretic action of bendroflumethiazide in one convenient medication. The two drugs complement each other

so that smaller doses of both are possible.

Rauwolfia combined with bendroflumethiazide is particularly effective in long-term therapy,<sup>15-17</sup> since beneficial effects do not diminish with continuous daily administration.

For most patients 1 or 2 Rautrax-N tablets daily are sufficient for maintenance therapy. The simplicity, convenience and economy of such a dosage schedule are of particular benefit to older patients.

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**Contraindications:** Severe renal impairment or previous hypersensitivity. **Warning:** Ulcerative small bowel lesions have occurred with potassium-containing thiazide preparations or with enteric-coated potassium salts supplementally. Stop medication if abdominal pain, distension, nausea, vomiting or G.I. bleeding occur.

**Precautions and Side Effects:** The dose of ganglionic blocking agents, veratrum or hydralazine when used concomitantly must be reduced by at least 50% to avoid orthostatic hypotension. Caution is indicated in patients with depression, suicidal tendencies, peptic ulcer; electrolyte disturbances are possible in cirrhotic or digitalized patients. Marked hypotension during surgery is possible; consider discontinuing two weeks prior to elective surgery and observe patients closely during emergency surgery. Rauwolfia preparations may cause reversible extrapyramidal symptoms and emotional depression, diarrhea, weight gain, edema, drowsiness may occur. Bendroflumethiazide may cause increases in serum uric acid, unmask diabetes, increase glycemia and glycosuria in diabetic patients, and may cause hypochloremic alkalosis, hypokalemia; cramps, pruritus, paresthesias, rashes may occur.

**Dosage and Supply:** Initial dosage, 1 to 4 tablets daily, preferably at mealtime. Maintenance, 1 or 2 tablets daily. Rautrax-N is supplied as capsule-shaped tablets containing 50 mg. Rauwolfia serpentina whole root (Raudixin®), 4 mg. bendroflumethiazide (Naturetin®), 400 mg. potassium chloride.

**Also available:** Rautrax-N Modified — capsule-shaped tablets containing 50 mg. Rauwolfia serpentina whole root (Raudixin), 2 mg. bendroflumethiazide (Naturetin), 400 mg. potassium chloride. Both potencies available in bottles of 100. For full information, see Product Brief.

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shock one can test for metabolic acidosis, the hemostatic breakdown or the massive vasoconstriction.

If one inserts a catheter in the subclavian or innominate vein, it is possible to obtain far more information regarding the stage of hemodynamic breakdown in shock and its proper management, than one can from arterial pressure, blood volume, or cardiac output determinations, because it is the amount of blood returning to the heart which gives the true index of the state of failure of the circulation. Not to be neglected in such an appraisal are the simple observations on the color and temperature of the fingers, the filling of the neck veins, and hourly urinary output. Such simple and valuable data, may render expensive multichannelled monitoring systems into a purely research rather than a clinical tool in appraising the state of the M.C.

The terminal vascular bed are the peripheral vessels having a diameter of  $100\mu$  or less. These vessels are by no means a homogeneous apparatus, since they consist of a large number of segments which do not react in the same direction nor simultaneously. Some contract as others are dilating and others remain unchanged. In this way one of its main objects, namely adequate tissue nutrition is achieved. This is accomplished by autoregulation<sup>2</sup> an intrinsic mechanism by which an organ is able to maintain a constant blood flow despite changes in arterial perfusion pressure. It is really a mechanism for maintaining nutrient flow when arterial pressure is reduced locally or systemically. For example, by postural changes, by arterial stenosis, or by decreased cardiac output or by hypotension of any sort.

Individual vascular areas will react differently to the same stimulus. For example we find that the microcirculatory response to stress will vary from organ to organ or even in the same organ depending on the basal vascular tone normally present in the precapillary resistance vessels and sphincters and also to a certain extent in the post-capillary vessels. By contrast the smooth muscles in the larger veins and the cutaneous arterio-venous anastomosis seem to exhibit little if any intrinsic activity under normal circumstances because they are controlled by sympathetic efferent vasoconstrictors.<sup>3</sup> Because of this sympathetic control of the larger vessels, maximal vasodilatation in the skin can be accomplished by reflex inhibition of sympathetic tone or actual section of the sympathetics. This cannot be accomplished in the brain, or the skeletal muscles or heart where residual basal tone is little affected by interruption of the vaso-motor nerves.

Capillary permeability enters importantly in the study of the microcirculation. When injury occurs a series of responses are observed leading to dif-

ferent types of vascular leakage. In addition should the capillary pressure fall below a critical level, (25 mm. Hg.) then cell clumping, silting or sludging develops to a point which partially or completely plugs the M.C. As the endothelium thus becomes ischemic, fibrinolysins are liberated which serve now to dissolve the microthrombi and help to desludge the terminal vascular bed, a beautiful example of what Cannon called "the wisdom of the body."

The Swedish workers Gelin, et al<sup>4</sup> showed that stasis in the M.C. after tissue injury can develop far away from the site of trauma in the post-capillary vessels and sinusoids which are the sites of the slowest flow and shear rate. This cell aggregation, they found, can be counteracted by dextran 40.

It is only a small step from a platelet aggregate to a platelet thrombus and then to a fibrin thrombus. The factors which accelerate this process, de Takats points out, are a decreasing capillary flow, a damage to the endothelial surface, and possibly a shift of the pH to the acid side. A widely disseminated intra-vascular microthrombus is found in a variety of clinical states.<sup>5</sup> This using up of available fibrinogen in widespread microthrombosis can result in the depletion of hemostatic components which can paradoxically enough lead to hemorrhage.

L.H.N.

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## Transplantation Biology: 1. An Important Technique In Biologic Research

The clinical aspects of the subject of transplantation have been responsible for focusing professional as well as public attention to this subject. However, there is a wide range of problems in genetics, embryology, physiology, oncology, etc. in which transplantation of cells, tissues, and organs provides a basis for powerful analytical study. In embryology, it is of course the classic method of studying the interaction of cells of different types as for example the process of induction. Growth substances have been discovered,<sup>1</sup> origin of tissues and organs have been elucidated. The manner in

which genes determine skin and hair color has been clarified in part by studies involving the incorporation through grafting of melanocytes with one genetic constitution into epidermal derivatives with a different one.

We have learned that there are striking functionally important differences between the epidermis of different regions of human skin. For example the exquisite transparency of that of the cornea, the toughness of that of the scales of the feet and the hardness of that of the nails. In order to determine the manner by which these differences are conserved throughout life requires grafting experiments in which epidermis from one region is artificially combined with dermis from another. These have shown the remarkable fact that with a few exceptions maintenance of the specificity of most types of epidermis is the outcome of persistent inductive stimuli from the underlying dermis.<sup>2,3</sup>

Among the techniques which have led to the elucidation of the role of the thymus in the development of immunological responses the important one has been transplantation. This has provided a good part of our knowledge of the life history of the small lymphocyte of the blood stream.

Then there is the problem of senescence. Do tissues have a finite life span or are they eternal as are presumably some of the unicellular organisms. One of the most important approaches to this problem involves the application of grafting to produce heterochronic chimeras, that is, individuals in which a particular organ or part of an organ is derived from a donor very much older or younger than the host. What such studies have shown to date is that tissues and organs alas are not eternal but have a finite life span however they are maintained. It should not come as a shock to us that when we eliminate cancer, arteriosclerosis, and thrombosis, the diseases presently responsible for most deaths in later life, that life is finite and we cannot in the end escape Father Time.

The discriminatory power of grafting techniques has been greatly sharpened by the introduction of markers which can be employed to follow the fate of transplanted cells. These include abnormal chromosomes, sex chromosomes, nuclear satellites of Barr bodies, isoantigens, enzymes and abnormal hemoglobin of red cells with a variety of radioisotope labels.<sup>2</sup>

As a means of evaluating tissue viability, transplantation is frequently superior to cultivation *in vitro*, since such explants normally lose their characteristic histological organization. For example, a piece of skin grafted to an appropriate site will not only establish cell survival, but it will survive as an organized functional tissue with its ancillary structures. Furthermore, if one wishes to appraise the ability of some tissues, cells, and

even organs to withstand certain treatments *in vitro* there is no better method than transplantation. In this way the effects of exposure to thermal and other stresses, as is encountered in the development of storage procedures, and exposure to drugs can be worked out and clarified.

There are a wide variety of grafts. First and foremost is the fertilized ovum, the implantation and development of which is a kind of transplantation. Then there are the single discrete cells such as those of tumors. Grafts may be suspension of cells in fluid media such as in blood and lymph. Or they may be solid tissue such as skin or cornea. They may be organs as complex as kidneys, livers, or heart. Finally, there is the grafting of the body of one individual onto that of another, known as parabiosis. All of these methods of transplantation have yielded fundamental biological information in profusion.

Even non-viable grafts of some tissues including bone and cartilage are now widely employed in replacement surgery, as indeed are blood vessel segments, heart valves fashioned entirely of synthetic polymers. Finally we cannot omit such allegedly inert grafts employed in contour remodeling. These are achieved by insertion of solid prostheses as well as by injection of fluids such as dimethyl-polysiloxane, techniques being practiced on an increasing scale by plastic surgeons. We do not have sufficient knowledge of the reactions of the host's tissues towards them. This is important because there always lurks the thought—will they prove oncogenic?

We thus can see that the field of transplantation biology because of its versatility as a tool in fundamental biological research, has great potentialities in other directions besides its clinical application which because of its promise to save lives must dominate the field for years to come.

L.H.N.

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## Science Tools: 21. Cinecoronary Arteriography

There are many questions concerning the coronary circulation that still remain unanswered. In what proportion of patients in whom we diagnose coronary artery insufficiency is coronary disease actually present? If coronary artery disease is



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present, in what part of the coronary tree is it located? If the coronary arteries are diseased, how much collateral circulation is present? How much actual flow is taking place through the coronary arteries? What is the rate of progression of sclerosis in a coronary vessel? If sclerosis is present, is it segmental or diffuse, does it involve the large arteries, the minute arteries, or both?

From the clinical standpoint other questions present themselves. Is it possible to have reduced coronary flow and yet have open large coronary arteries? How much flow is added to the coronary circulation when an internal mammary artery is implanted? Even if flow is added to large vessels, how much of this becomes available for cellular perfusion and how much runs off through large connecting channels which add nothing to cellular perfusion? Do revascularization procedures of the myocardium add anything to the present management of coronary artery disease?

Confusion in the answers to many of these questions is rampant. Some surgeons report brilliant results with operations to improve the coronary circulation. Some prominent surgeons claim they have never seen sclerosis of the internal mammary artery when employed to revascularize the myocardium. Other surgeons have given up transplanting the internal mammary because it is too often sclerosed! One is quoted as insisting his operation of transplanting the internal mammary artery perfused the coronaries within hours after the operation! At the moment no sound and proved studies have been carried out in human beings to show the benefits derived from the numerous procedures now being applied to revascularize the human heart.

The introduction of the cinecoronary arterial visualization should add much information towards answering the above questions. The method requires cutting down on and cannulating the brachial artery—passing the catheter into the left ventricle, injecting a dye which results in clear outlines of the large coronary arteries. One can detect by the cine method narrowing, constriction, obstruction, anomalies and also the existence of collateral channels. The pictures are quite striking and groups are springing up all over the country to learn what they can by this method about coronary artery disease.

No one can deny that this type of study represents an advance but like all new methods it has created excessive enthusiasms, much of which unhappily will be muted by further experience. One surgeon already claims that medical diagnosis of coronary artery disease is on its way out because one-third of all cases so diagnosed were found by cinecoronary arteriography to have normal coronary

arteries! Another insists that the technique will render the electrocardiographic diagnosis archaic! What are the real facts.

As carried out now cinecoronary arteriography has very definite limitations. It tells nothing of the small coronary arterioles or small vessels. If one compares an injection of the coronary arterial tree with a barium latex mixture of standardized particle size with the cinecoronary arteriogram, one will see hundreds of vessels which are not studied by the latter technique. This does not take into account the progressive constriction of the coronary tree after death which must have obscured many more small vessels that were open during life and not visualized by the cine method. No one can deny disease does occur in these vessels and this might account for a large part of the one-third claimed not to have angina because of normal coronary arteriograms.

Furthermore cinecoronary arteriography tells one nothing about coronary arterial flow. The mere fact that a vessel can be injected and seen does not necessarily mean that any significant perfusion of a myocardial segment is being carried out, because the small vessels are blanked. Even if a 50 per cent narrowing of a vessel is discovered this fact alone does not necessarily imply that flow is diminished. To establish the fact one must devise a method of differential flow to supplement this technique.

The technique also tells us absolutely nothing about what is taking place at the cellular level which is so exquisitely defined in characteristic electrocardiographic changes. To determine what is occurring at the cellular level may well prove to be the most profitable approach to study of the coronary circulation. Cinecoronary arteriography may show one to have excellent coronary arteries, but the myocardium may be studded with fibrosis and there may be advanced myocardial disease.

Zimmerman and Demany<sup>1</sup> describe the case of a 46 year old pilot who is found at the time of his yearly physical examination to have a left bundle branch block, a finding not present on his previous examination. Selective coronary angiography showed his arteries to be perfectly normal. His left ventricular end-diastolic pressure however was high—28 mm Hg—clearly this patient had primary myocardial disease. The cinecoronary arteriographic enthusiast would have claimed a normal heart for this patient.

But this is not all. The technique itself is not without danger and may be catastrophic. There are case reports of ventricular fibrillations and even deaths from the procedure though these are rare. Even a reversible ventricular fibrillation is not to be taken lightly. The fact is, the procedure is highly specialized and demands that strict attention be

paid to meticulous carrying out of the technique if one is to avoid serious complications. One element is to use a type of contrast media with a very low sodium content.

Then there is the radiation hazard to which very little attention has been paid. In the making of multiple selective coronary visualizations rather large doses of x-rays are directed to the patient's heart. Conservative estimates of total radiation to the patient's heart during the procedure approximates 40-80 Roentgens.<sup>1</sup> One six foot chest x-ray film averages .007 Roentgens. What the physiologic results are from the irradiation to the heart in an acute form and on a long range basis have not been studied. Obviously the effect on a diseased heart could be even more serious.

Finally, we must not forget the possibility of injury to the brachial artery and the radial nerve during the act of cannulation with resulting morbidity.

Hence coronary artery visualization is not to be taken for granted. Its use must have a good basis in sound clinical judgment. It will not dispense with the doctor. It will not relegate the electrocardiogram to the Smithsonian Institution. For the present it must remain in the experimental realm as a procedure designed to study the large coronary arterial tree. In the clinic it is a procedure that must be used with caution and normal visualizations are not to be taken as in any way ruling out an impaired coronary blood flow.

L.H.N.

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### Ovulen—A New Oral Contraceptive

Ovulen (Searle), the newest oral contraceptive, is described in advertisements as "a significant chemical advance" offering "protection at a new low dosage." The estrogenic component of Ovulen is mestranol (0.1 mg per tablet), which is present at the same dosage in other oral contraceptives. The progestin component, ethynodiol diacetate (1 mg per tablet), is most closely related to the norethindrone compounds (Ortho-Novum—Ortho; Norlestrin—Parke, Davis; Norinyl—Syntex). The "low dosage" claim, like almost all claims based on differences in milligram potency, is meaningless.

In several studies, Ovulen has proved to be as effective as other oral contraceptives. Whether there is a lower incidence of common side effects, such as nausea, weight gain, breakthrough bleed-

ing or chloasma with Ovulen can be determined only with wide and prolonged use.

### COMPARISON WITH SEQUENTIAL THERAPY

The promotional literature for Ovulen claims that combined progestin-estrogen contraceptive tablets have greater efficacy than the sequential tablets (C-Quens—Lilly; Oracon—Mead Johnson), which provide estrogen alone for the first 15 or 16 days of the cycle and both progestin and estrogen for only the last five days. This claim appears to be valid. The Medical Letter has pointed out that omission of one tablet of a sequential contraceptive is more likely to result in pregnancy than omission of a combination tablet (Medical Letter, Vol. 7, p. 77, 1965). There is also some belief that the sequential tablets are not as reliable as the combination tablets, even when no doses are missed. A World Health Organization Scientific Group states: "The effectiveness of currently used combined oestrogen/progestogen oral contraceptives is reflected in a pregnancy rate of not more than 0.1 per 100 women-years of use if the contraceptives are taken according to instructions. . . . The effectiveness of the currently available sequential regimens appears to be somewhat less" (WHO Techn. Rep. Ser. No. 326, p. 17, 1966).

### ORAL CONTRACEPTIVES AND LIVER DISEASE

Impairment of hepatic function is probably frequent with all of the oral contraceptives, including Ovulen, but it is clinically insignificant. G. J. Kleiner et al. (*New Eng. J. Med.*, 273: 420, 1965) and others have observed increased bromsulphalein retention in patients on Enovid and Enovid-E (Searle). The retention was believed to be related to interference by the progestin with the transfer of the dye conjugates from the liver cell into the bile; the abnormality was uniformly reversible in studies, and microscopic and histochemical examinations of liver biopsies from these patients were all normal. No harmful effects have been seen even in those women in whom jaundice has developed from other causes and in whom the medication has been continued. The only hepatic disorders which should be considered a contraindication to the use of oral contraceptives are previous cholestasis of pregnancy, primary biliary cirrhosis, and hereditary disorders of hepatic excretory function such as the Dubin-Johnson and Rotor syndromes. No evidence has been presented that preexisting liver damage increases the susceptibility of the bile secretory apparatus to impairment by contraceptive drugs.

*Reprinted from The Medical Letter on Drugs and Therapeutics, New York, N.Y. Vol. 8, No. 16, August 12, 1966.*



# James Gates Percival (M.D. Yale 1820)

## Once Our Nation's Most Promising Poet

Thomas E. Cone, Jr., M.D.

■ Perhaps no physician in our nation's history has been so versatile and so eager in the acquisition of learning and yet has been so forgotten as James Gates Percival (Fig. 1). Few will recognize his name although he was our most famous poet during the 1820's and early 1830's, a position he held until the ascendancy of William Cullen Bryant. The versatility of this remarkable physician is staggering when one discovers that during his lifetime he distinguished himself in medicine, poetry, geology, linguistics, philology, law, teaching, anatomy, botany, and newspaper editing.

Percival was born in Kensington, Connecticut on September 15, 1795 in a house still standing, although somewhat altered from its original appearance (Fig. 2). Here, known as a shy, sensitive child with an omniverous taste in reading, he spent his boyhood. He became exceptionally well informed in



FIGURE II

Percival's boyhood home in Kensington, Connecticut as it appeared a few years ago. (Reproduced through the Courtesy of Dr. Herbert Thoms, Stony Creek, Connecticut).

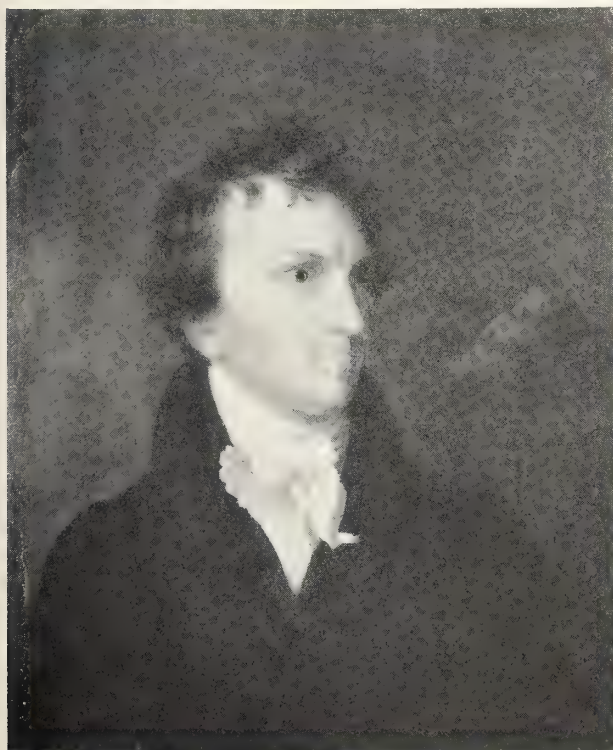


FIGURE I

Oil Portrait of Dr. James Gates Percival (1795-1856) painted by Francis Alexander probably in 1825. (Reproduced through the Courtesy of the Yale University Art Gallery, Gift of Harvard University).

geography and when only 14 years of age wrote an epic *The Commerciad* which was a versified gazetteer.<sup>1</sup>

When he was 16 years old he entered Yale College where he proved to be a brilliant although temperamental scholar, intolerant of any criticism. Because a few of his classmates ridiculed his attempts at writing poetry, he withdrew temporarily from college in his second year, returning to his home village to teach in a district school. Fortunately he returned to Yale the following year and delved intensely into chemistry and minerology under the elder Benjamin Silliman and into botany under Eli Ives. He also gained a reputation in New Haven literary circles as a promising and talented young poet.

In 1815 when he graduated with honors, President Day of Yale said of Percival:

"he was among the most distinguished in his class in talents and literary acquirements."<sup>2</sup>

In 1820 Percival received his M.D. at Yale once again distinguishing himself as a student. Dr. Ives, Professor of Materia Medica and Botany in the

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DR. THOMAS E. CONE, JR., Professor of Pediatrics, Southwestern Medical School, Dallas, Texas.

newly established Yale Medical School, lauded Percival's scholarship in these words:

"He is an excellent scholar, and as a naturalist is scarcely excelled by any person of his age in the United States. As a medical scholar I may safely say that from the commencement of the Medical Institution (Yale), no one in the examination for the degree of Doctor of Medicine has appeared better than Dr. J. G. Percival."<sup>3</sup>

Percival returned to his home village to practice medicine and within a few months had developed an extensive practice. But one day, five of his patients died suddenly of an unexplained fever in spite of his vigorous efforts to save them. Discouraged by this unfortunate incident he abruptly ended his practice, saying to a fellow physician that he could not bear to have people looking to him for relief and to be unable to relieve them.

In 1821 Percival gained wide recognition overnight as a poet upon the publication at his own expense of *Poems* which included the long Spenserian "Prometheus," acclaimed by his compatriots as the equal of Byron's *Childe Harold*. Many literary critics hailed his poetic gifts as the most classical in America. The appearance of *Clio I* and *II* in 1822 and of *Prometheus, Part II with Other Poems* the same year further enhanced his literary fame.

Percival was indeed held high in the eyes of most of the literary giants of his day as is evident from Whittier's comment in 1830 in the *New England Review*:<sup>4</sup>

"God pity the man who does not love the poetry of Percival. He is a genius of nature's making—that singular and high minded poet."

Yet, in spite of such praise our literary tastes have so changed that not a single one of Percival's poems is to be found in any of the standard current anthologies of American poetry. One of the best known of Percival's poems memorized by most school children, especially in New England, in the period prior to our Civil War was titled *New England*. The first two stanzas of this poem are excellent examples of the flavor of Percival's poetic style.

#### NEW ENGLAND

Hail to the land whereon we tread,  
Our fondest boast!

The sepulchre of mighty dead,  
The truest hearts that ever bled,  
Who sleep on glory's brightest bed,  
A fearless host:

No slave is here;—our unchained feet  
Walk freely, as the waves that beat  
Our coast.

Our fathers crossed the ocean's wave  
To seek this shore;  
They left behind the coward slave  
To welter in his living grave;  
With hearts unbent, high, steady, brave,  
They sternly bore  
Such toils as meaner souls had quelled:  
But souls like these, such toils impelled  
To soar.

His petulance and tactlessness as the Phi Beta Kappa orator at Yale in 1825 coupled with his sudden and unexpected resignation as editor of Bond's *American Athenaeum* the same year provoked a storm of newspaper disapproval which so upset Percival that he withdrew abruptly from his literary career, publishing only *Clio No. III* (1827) and *The Dream of a Day and Other Poems* (1843) during the remainder of his lifetime.

Percival vacillated between several totally unrelated careers after foregoing literature. He assumed the editorship of the *Connecticut Herald*, but regarded this task as an insult to his intelligence which may explain why the *Herald* failed. Through the influence of John C. Calhoun, the Secretary of War, Percival obtained a professorship in chemistry at West Point, but he soon wrote that he hated chemistry so much that the very thought of it gave him an ague. After a few months of being miserably unhappy as a chemist, he asked to be transferred to the office of Post Surgeon in Boston, but service as a physician examining recruits was not to his taste either; he once again gave up the practice of medicine, this time for good.

One of Percival's many hobbies was the systematic study of languages. His linguistic attainments and thorough knowledge of more than 12 languages led to his collaboration with Noah Webster for a year or two in revising the manuscript of *An American Dictionary of the English Language* (1828).

No career gave Percival satisfaction for long. Thoms<sup>5</sup> has written:

"His innate ability rose at times to sheer genius and the one thing that prevented his occupying a foremost place in American letters was the peculiar psychology with which he was unfortunately endowed: a nature in which petulance, lack of judgment, instability and ill health were ever present—that group of nervous phenomena which seems to be almost universally the penalty of genius."

Perhaps, it was as a geologist that this man of many talents did his most lasting scientific work. In 1835 he was appointed state geologist of Connecticut; in 1842 he published his "Report on the Geology of Connecticut," which took him more than five years of concentrated effort to complete.



He could not be paid for his survey until it had the governor's approval but Percival's intransigence led him to refuse to submit the report to the governor, whom he considered incompetent to judge the value of his report.

Poverty-stricken as a result of his unpaid work as a geologist and his lavish purchases of books, he voluntarily secluded himself in three unswept rooms in the State Hospital in New Haven, where he lived alone, engaged occasionally during the next ten lonely years as a railroad surveyor and geologist.

From the director of the hospital at this time we learn the few details that are known of his lonely life. No one was allowed to enter his rooms; he would not invite visitors as distinguished as the poet Longfellow into the living quarters. Percival would often forget to eat for days and when he did his meals were of the simplest nature—crackers, herring and dried beef. Although he was unyielding and eccentric, utterly impractical, living alone with his 10,000 books, he was nevertheless one of the most learned men of his time.

Percival's geological reports brought him so high a reputation as a geologist that he was engaged temporarily by the American Mining Company to investigate the lead deposits in Wisconsin. While making such a survey he died unexpectedly in the small town of Hazel Green, Wisconsin, on May 2, 1856.

Not having made a will, he became in death, as in life, a further object of public clamor. His physician claimed his estate. The New Haven city

council refused to defray the cost of burying the poet in that city, and public subscription to purchase and place his library at Yale as a memorial did not succeed.

Percival lies buried in Hazel Green where many years later a group of friends erected a monument on which is inscribed the following tribute:

EMINENT AS A POET  
RARELY ACCOMPLISHED AS A  
LINGUIST  
LEARNED AND ACUTE IN SCIENCE  
A MAN WITHOUT GUILE

He surely deserves greater recognition than he received since his death. He may not have been a great physician, but he certainly brought fame to our profession, not only during the years when he was the nation's chief poet, but also in the exceptional talent this most versatile physician brought to the many other careers he pursued with such distinction.

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6. Ward.<sup>2</sup> p. 463.

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"In the trajectory of a human life, there is a brief span in which the unspent vigor of youth overlaps with the accumulated experience and wisdom of maturity. For most of us, if this brief golden moment comes at all, it comes between 40 and 50." Arnold J. Toynbee, British historian, "Churchill—Progress of a 'Slow Grower'." *The New York Times Magazine*, November 1, 1964; p. 40.

# The Management Of Bacterial Shock And Septic Abortion

Leon Speroff, M.D. and Clarence D. Davis, M.D.

## Clinical Features

Essential criteria for the diagnosis of bacterial shock are the presence of a bacterial infection and hypotension not related to blood loss. The temperature is usually elevated above 101° F. orally, however subnormal levels are frequently seen prior to, or associated with, the onset of shock. Chills, pallor, and respiratory distress are common characteristics. A foul vaginal discharge and a tender uterus are important findings in the obstetrical patient. The mental status of the patient is frequently that of striking clarity and may lull one into a sense of false security. A significant number of patients have warm, dry skin which may be misleading. Jaundice, cyanosis, cardiac arrhythmias and/or uremia suggest a grave prognosis.

Leukopenia in the early stages is soon followed by leukocytosis. The hematocrit is usually normal, but the platelet count may be low, suggestive of intravascular clotting. Electrolytes are usually consistent with a metabolic acidosis.

In most cases a traumatic procedure can be related to the onset of bacterial shock. In a series of 169 cases, 82 per cent had genitourinary procedures.<sup>9</sup> In 20 cases seen over a 6 year period in the Department of Obstetrics and Gynecology of the Yale-New Haven Hospital, the majority were related to pregnancy (Table I). Only 4 of the 10 septic abortions admitted interference, but it is wise to assume

TABLE I  
BACTERIAL SHOCK IN OB-GYN  
YALE-NEW HAVEN HOSPITAL  
JAN., 1960-DEC., 1965

|                        | SURVIVED | DIED |
|------------------------|----------|------|
| Septic Abortion        | 7        | 3    |
| Chorioamnionitis       | 1        | 2    |
| Postoperative:         |          |      |
| Vaginal Hysterectomy   | 2        | 0    |
| C-section Hysterectomy | 0        | 1    |
| Appendiceal Abscess    | 0        | 1    |
| Sigmoid Fistula        | 1        | 1    |
| Pyelonephritis         | 0        | 1    |
| Total                  | 11       | 9    |

(45% mortality)

*From the Department of Obstetrics and Gynecology of the Yale University School of Medicine and the Yale-New Haven Hospital, New Haven, Connecticut.*

TABLE II  
ORGANISMS ISOLATED IN BACTERIAL SHOCK IN OB-GYN  
YALE-NEW HAVEN HOSPITAL  
JAN., 1960-DEC., 1965

|                         | SURVIVED | DIED |
|-------------------------|----------|------|
| E. coli                 | 1        | 6    |
| E. coli plus:           |          |      |
| Clostridium welchii     | 2        | 1    |
| Pseudomonas             | 0        | 1    |
| Proteus                 | 1        | 0    |
| Klebsiella-aerobacter   | 2        | 0    |
| Pseudomonas             | 2        | 0    |
| Anaerobic Streptococcus | 1        | 0    |
| Negative Report         | 2        | 1    |
| Total                   | 11       | 9    |

that where there is fever there most likely was interference. Gram negative organisms are most commonly isolated as seen in Table II.

## Physiology Of Endotoxin Shock

Hypotension due to endotoxin is associated with a decreased cardiac output because of a decreased venous return as a consequence of pooling of blood in the splanchnic bed (Figure 1). Endotoxin has a sympathomimetic effect, particularly in the visceral organs and apparently more intense on the venous side of the circulation. Unless there is significant blood loss there is no critical change in blood volume and the central venous pressure remains normal or slightly decreased (barring cardiac damage or failure). A further effect of endotoxin is the precipitation of widespread intravascular clotting—the Shwartzman phenomenon (Figure 1). In some unknown way, pregnancy “prepares” for the Shwartzman reaction so that the initial exposure to endotoxin has a thromboplastic effect. This may be complicated by significant fibrinolysis.

## Treatment Of Bacterial Shock

### GENERAL MEASURES

1. Cultures of blood, urine, wounds, and cervix when indicated. Gram stain smears may facilitate

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## PHYSIOLOGY OF ENDOTOXIN SHOCK

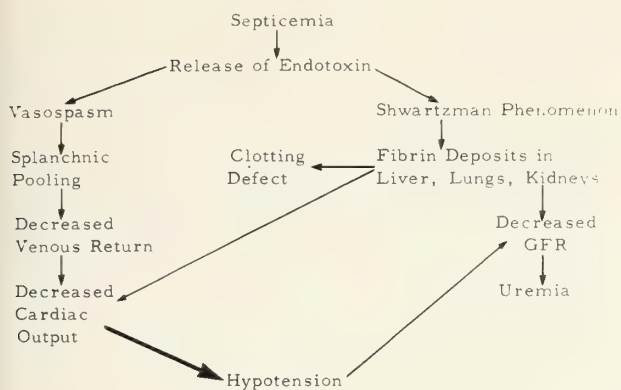


FIGURE I

Schematic representation of the physiology of endotoxin shock.

an early diagnosis with a more intelligent selection of antibiotics.

2. Blood studies: complete blood count, blood urea nitrogen, electrolytes, fibrinogen, prothrombin time, liver function tests, platelet count, clot formation and stability, type and cross-match.

3. Baseline electrocardiogram.

4. Chest and abdominal x-rays to rule out foreign body, gas formation, sub-diaphragmatic air or masses.

5. Foley catheter: Delay in the insertion of an indwelling catheter into the bladder may result in the failure to recognize oliguria. Hourly urine output and specific gravity should be charted along with frequent vital signs and strict I. & O. Intravenous mannitol in a 10 per cent solution is given if the urine output falls below 30 cc./hour.

6. Central venous pressure readings: A polyethylene catheter is threaded via an antecubital vein into the subclavian vein or the superior vena cava. Continuous central venous pressure is then readily followed and should be kept between 30 and 120 mm. water. IV fluids can be administered by using a three-way stopcock at the bottom of the manometer. Blood transfusion is not indicated except to replace blood loss. Plasma or plasma expanders may be used to maintain a normal central venous pressure. If the central venous pressure is high with persistent hypotension, rapid digitalization is indicated.

7. The metabolic acidosis is best treated with IV sodium bicarbonate. It should be noted that respiratory alkalosis may mimic acidosis with a compensatory hyperventilation.

### ANTIBIOTICS

In our experience the treatment of choice is the simultaneous use of the following: 1. IV penicillin—60-80 million units per 24 hours. (note: 1.5 mEq.

potassium per 1 million units). 2. IV chloramphenicol—3-6 grams per 24 hours. 3. IM streptomycin—1.0 gram immediately and 0.5 gram every 12 hours. (less in the presence of oliguria).

Such massive doses of penicillin are usually effective against all gram negative organisms except *Pseudomonas*. Reactions include central nervous system irritation and hyperkalemia. A sodium salt of penicillin is available and should be used when there is renal damage. Early chloramphenicol toxicity may be detected by a decreasing reticulocyte count.

### VASOPRESSORS

In view of the physiology of endotoxin shock, vasopressors may be undesirable, producing excessive vasoconstriction with secondary ischemia. Nevertheless higher survival rates are found with use of vasopressors,<sup>8,9</sup> and in our experience a favorable response with an increase in blood pressure and urine output is usually seen.

Metaraminol (Aramine) and levarterenol (Levophed) are the agents of choice because of their inotropic action on the heart. These vasopressors are given intravenously in concentrated solution, titrating the rate of administration against the systolic blood pressure, maintaining a level of at least 90 mm. mercury. The use of phentolamine (Regitine) in conjunction with levarterenol (5 mg. to 1 ampule) is recommended to avoid local tissue injury.

### VASODILATION

The main effect of peripheral vasospasm with splanchnic pooling seen with endotoxin is blocked by anti-adrenergic measures. If the blood flow through the visceral organs can be reestablished, increased venous return and cardiac output will stabilize the blood pressure. Recently the use of vasodilating agents for this purpose has been advocated.<sup>3</sup>

Phenoxybenzamine (Dibenzylin) in a dose of 1 mg. per Kg. body weight increases the renal blood flow and urine output with a resultant increase in survival rate.<sup>3,6</sup> Other agents used with similar results are chlorpromazine (Thorazine)<sup>2</sup> and isoproterenol (Isuprel).<sup>4</sup> Chlorpromazine is given in 10-25 mg. doses IV every 4-6 hours as indicated.

Isoproterenol increases the rate and force of cardiac contractions and at the same time is a vasodilator. It is given intravenously (diluted 1 mg. in 500 cc. solution) keeping the pulse under 110. A pulse of 130 or more may precipitate cardiac arrhythmias and hence decrease stroke volume.

Recently we had a case of bacterial shock following a septic abortion which was unresponsive to steroids and metaraminol. The response to isoproterenol was dramatic. The patient survived

despite 24 hours without a recordable blood pressure prior to the use of isoproterenol. This case will be reported in detail elsewhere.<sup>1</sup>

If vasodilating agents are used, the central venous pressure must be maintained in the normal range before and during administration. Certainly vasodilatation is contra-indicated in hypovolemia.

#### STEROIDS

There is a greater survival rate in those patients receiving high doses of steroids.<sup>3,5,7,9</sup> The dosages should be massive: 50 mg. hydrocortisone or 2 mg. dexamethasone (Decadron) per Kg. body weight per 24 hours by slow IV drip. Such doses apparently have an inotropic action resulting in increased cardiac output, and there is also a vasodilatation effect with a decrease in peripheral resistance.<sup>3</sup> Acute gastrointestinal ulceration may be a significant side effect even if the treatment is limited to a short duration (48 hours). Tapering is not necessary.

#### ADDITIONAL PROCEDURES

Hypothermia is beneficial in reducing oxygen requirement, reducing very high fevers, and in exerting a cold pressor effect. Chlorpromazine 10-25 mg. IV) may be used to inhibit shivering which is painful and generates heat.

The use of heparin (50 mg. every 8 hours by IV drip, in a separate bottle to prevent neutralization of the heparin by other medications) might be considered if intravascular clotting is significant (low fibrinogen, prolonged prothrombin time, and low platelets). Aminocaproic acid is indicated if fibrinolysis becomes a complication (5.0 grams diluted in dextrose and water given over a 1 hour period, then a continuous infusion at the rate of 1.0 gram per hour).

### The Surgical Management Of Septic Abortion

Patients with septic abortions are always potential candidates for bacterial shock. Since the sine qua non in the treatment of bacterial shock is the removal of the source of infection, early surgical intervention in patients with septic abortions is frequently life-saving.

Early curettage with liberal use of oxytocin (1-10 cc. per liter as indicated) is employed when:

1. the uterus is relatively small (12 weeks' size or less).
2. a good circulating antibiotic level has been obtained.
3. if the patient's clinical condition is stable.

Occasionally curettage is followed by chills and a sharp rise in temperature, but even then recovery seems to be more rapid.

The patient in whom curettage is inadvisable may be a candidate for hysterectomy. The decision

to proceed with hysterectomy is not an easy one as the criteria are not clearly fixed. Furthermore the decision is influenced by the parity of the patient. A more conservative approach may be justified in the patient who desires more children. However in the patient in whom reproduction is unimportant, especially multiparas with a history of previous septic abortions, consideration should be given to hysterectomy as the primary treatment.

In our experience the following indications for hysterectomy seem to be reliable:

1. attempted abortion with recent intrauterine injection of certain chemicals (e.g. soap, detergents, turpentine).
2. clinical deterioration (unremitting high temperature, falling blood pressure, oliguria) especially with a persistently tender uterus or foul vaginal discharge.
3. a large tender uterus, especially with a closed cervix or evidence of intrauterine sepsis due to *Clostridium*.

In the occasional patient where preservation of reproduction is important curettage might be performed rather than hysterectomy. It is too late to wait until jaundice, renal failure, or hemolysis intervene. Bilateral salpingectomy should accompany hysterectomy as marked acute salpingitis has been a prominent feature on histological examination.

Obviously individualization of surgical treatment is necessary, and only the physicians at the bedside can make the proper decisions. Delay in aggressive action, however, is likely to be as lethal as unwarranted interference.

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# Ovarian Pregnancy: A Case Report

Mark Solomkin, M.D., Mary M. Allen, M.D. and Stanley W. Edelstein, M.D.

■ Ovarian pregnancy is a rare phenomenon which usually terminates in early rupture of the pregnant mass.<sup>1</sup> However, the literature does contain reports of the pregnancy going to term<sup>2</sup> with the eventual formation of a lithopedion indicating the ability of the ovary to accommodate itself to the growing mass.

It is generally accepted that Spiegelberg's<sup>3</sup> criteria be fulfilled in order to maintain the diagnosis of ovarian pregnancy. These are: "(1) that the tube on the affected side be intact; (2) that the fetal sac occupy the position of the ovary; (3) that it be connected with the uterus by the ovarian ligament; and (4) that definite ovarian tissue be found in its wall."

The present case concerns a twenty-seven year gravida II para I. The patient was first seen by her family doctor in approximately her eighth week of gestation. Not much can be learned about the interval from the eighth to the twenty-first week except that she had repeated episodes of "abdominal pain." Beginning in the twenty-first week of her pregnancy and during the remaining weeks of gestation she exhibited recurrent episodes of "extensive and "severe abdominal pains" from which she couldn't "straighten up" associated with marked "anemia" and "acidosis." Her hemoglobin was reported at one time to have gone as low as "5.2 grams per 100 ml." She was treated "conservatively." This consisted of repeated episodes of hospitalization, intravenous fluids and massive whole blood transfusions. In the 38th week of gestation the fetal heart tones were lost. When labor did not ensue within three weeks, an unsuccessful attempt at medical induction was made. About ten days later the patient was again hospitalized for "acidosis" resulting from "severe nausea and vomiting." This was treated conservatively and symptoms subsided. About one week later the patient began to bleed vaginally and was hospitalized and again an unsuccessful attempt was made at medical induction. X-ray examination at this time reported: "(1) fetal death; (2) extra-uterine pregnancy?" At this time we were asked to see the patient in consultation. Because of the marked abdominal tenderness, examination was carried out under anesthesia. She was found to have a "long, closed, hard cervix." Just above the cervix there was a

fixed mass about 7-9 cm. in diameter. Posterior and extending from the left toward the right was another large fixed mass. The final conclusion was that the posterior mass probably represented an intra-abdominal pregnancy and arrangements were made for laparotomy. At laparotomy the peritoneal cavity was found to be filled with massive adhesions involving the bowel, the uterus, the uterine ligaments, the right ovary, the pregnant mass, and the parietal and the visceral peritoneum of the pelvis and the lower abdomen. When these were separated, the uterus was found to be on the upper limits of normal and levorotated. The pregnancy mass was found posterior to the uterus and extending from the left to the right. It was attached to the pelvic wall by the left infundibulopelvic ligament and attached to the rotated uterus by the left ligament of the ovary. It was removed separately. The left tube was identified "lying on the mass." Because of the extent of the rough and bleeding areas left by the separation of the adhesions total abdominal hysterectomy and right salpingo-oophorectomy was then done. The post-operative course was uneventful and the patient left the hospital on the sixth post operative day.

The pathologist's report identified the intact fallopian tube with "diffuse adhesions to the mass." The "ovary" was described as being "adjacent" to the tube and on examination was found to be part of the "wall of the mass." The possibility that this might have been an intra-abdominal pregnancy but not ovarian was considered but rejected because of ligamentous attachments. The following photographs taken after surgery are of interest and help demonstrate the pathology. Photograph No. 1 shows the relationship of the pregnancy mass to the genitalia. The left tube can be made out on top of the mass. Photographs No. 2 and No. 3 illustrate the position of the fetus in the mass and its relationship to the placenta. Microphotographs Nos. 4, 5, and 6 showing decidual tissue and ovarian tissue were taken from the same slide."

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*This report in part was aided by a grant from the Mark and Ruth Solomkin Foundation, Inc.*

### Summary And Conclusions

A case of ovarian pregnancy in which the fetus lived to the thirty-eighth week of gestation is reported. Recurrent episodes of marked anemia, severe nausea and vomiting are believed to have re-

sulted from repeated intra-abdominal hemorrhages from the pregnant mass. Spiegelberg's criteria for the diagnosis of an ovarian pregnancy were fulfilled.

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FIGURE I. Gross Specimen.



FIGURE II. Fetus In Amniotic Sac.



FIGURE III. Relation of Fetus to Placenta.

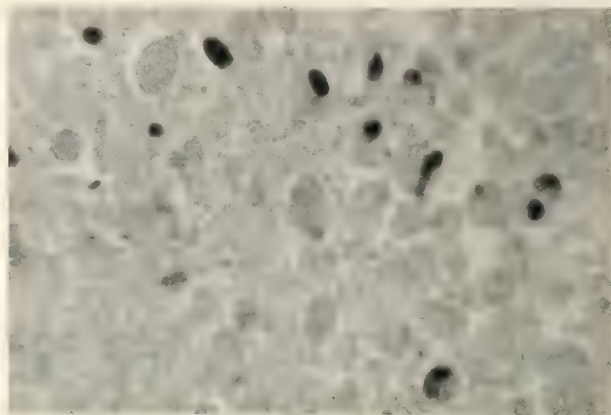


FIGURE IV. Decidual Tissue from section of Ovary.



FIGURE V. Decidual Tissue from section of Ovary.

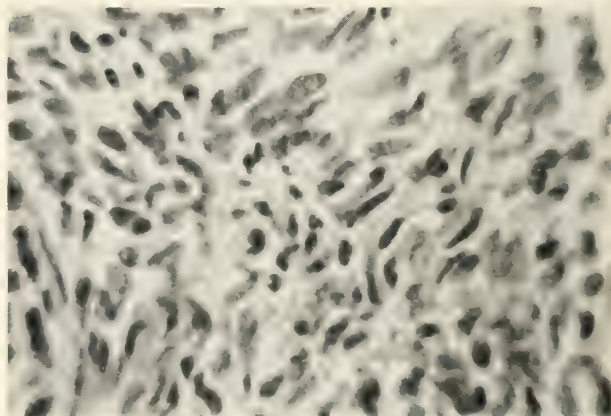


FIGURE VI. Section showing Ovarian Tissue.



# Candida Peritonitis

Bernard S. Shapiro, M.D.

## Introduction

■ *Candida* peritonitis is a complication rarely encountered in surgical practice. Only one other case has been reported in the literature to date.<sup>1</sup> With the increasing use of broad spectrum antibiotics it can be expected to be seen more frequently in the future. At the present time Amphotericin B is available for parenteral use as an effective fungicide, but this drug carries its own morbidity and side effects. The following case is presented to highlight the occurrence of a virulent *Candida* peritonitis and its successful treatment with intravenous Amphotericin B.

## Case Report

On July 14, 1965, an 18 year old white male was admitted to The Griffin Hospital Emergency Room with a gunshot wound of the upper abdomen accidentally incurred with a .38 caliber pistol approximately 10 to 15 minutes earlier. His past history and system review were entirely negative. Physical examination showed an acutely ill white male in severe pain with a blood pressure of 90/40 and a pulse of 140. Positive findings were limited to the abdomen. There was a wound of entrance in the mid-axillary line at the eighth interspace on the left side with the wound of exit in the posterior axillary line at the eighth interspace on the right side. Bowel sounds were absent. The abdomen was rigid. After sedation, initiation of fluid and blood replacement, and emergency chest x-ray to substantiate the clinical impression that the pleural cavities were spared, he was taken to the Operating Room.

Under general anesthesia through a bilateral subcostal incision, the course of the projectile was determined. There was a stellate laceration of the spleen, an entrance wound at the greater curvature of the stomach and an exit wound at the lesser curvature. The left hepatic artery was transected, and the right lobe of the liver was the seat of a penetrating jagged wound which led to the exit wound between the eighth and ninth ribs. Splenectomy, two gastrotomies, and ligation of the left hepatic artery were accomplished with stabilization of the blood pressure. The liver wound was handled by placing two large cigarette drains—one in the right superior hepatic space and one in the right inferior hepatic space—and bringing them out through the wound of exit which was debrided at that time. Two other cigarette drains were placed—one at the cardia and one in the splenic bed—and brought out through a stab wound below the left sub-coastal incision. He received 3,000 cc. of whole blood while on the operating table and arrived in the Recovery Room in a stable condition.

\* From the Surgical Service, the Griffin Hospital.

Postoperatively he was placed on penicillin and chloramphenicol. He required an additional blood transfusion daily for the next three days, but by the 5th post-operative day he was stable, taking adequate fluids orally, and afebrile. On the 7th post-operative day he spiked a fever of 102.8°F. and began to produce copious amounts of bile stained fluid through both drain sites. Gram stain and culture of this fluid showed *Candida albicans* growing in pure culture. Fecal gram stains and cultures showed gram negative rods identified as coliform organisms with rare yeast cells present. Blood and urine cultures were negative. Fresh smears from the drain site showed yeast forms with hyphae. Antibiotics were stopped on the 7th post-operative day and a tentative diagnosis of *Candida* peritonitis established. When on day eight his temperature persisted and bacteriologic recheck confirmed the earlier report, it was felt that active therapy was indicated.

Intravenous Amphotericin B therapy was instituted on the 22nd of July; 48 hrs. later the patient was afebrile with the exception of a temperature spike following the onset of the daily intravenous drip. Daily shaking chills and high fever persisted despite premedication with aspirin and sparine. Addition of cortisone helped ameliorate the shaking chill. With subsidence of the fever, drainage diminished and no yeast cells were obtainable from any subsequent cultures. Blood Urea Nitrogen determination remained within normal levels but climbed on the eighth day of therapy to 19 mg/100 ml and on the ninth day to 25. When therapy was stopped the BUN returned to normal levels in 48 hours.

The drains from the left side were slowly removed as drainage ceased but drainage persisted on the right side, yielding approximately 500 to 600 cc. of bilious fluid in a 24 hour period. By August 2nd all parameters showed marked improvement with the exception of persistent biliary drainage and acholic stools. X-ray attempts to visualize a fistula by oral and intravenous cholecystography and cholangiography were futile. Hypaque injection of the fistulous opening showed no direct communication with the extrahepatic biliary tree. Serum bilirubin levels were within normal limits.

On the 19th of August the patient was again taken to the Operating Room and explored through a right paramedian incision. The common hepatic duct was found to be bound down and obstructed by scar tissue. Lysis of this dense scar tissue was accomplished, and an operative cholangiogram at that time revealed a patent extrahepatic biliary system with a fistulous communication from a lesser branch of the right hepatic duct.

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DR. BERNARD S. SHAPIRO, Assistant attending surgical service, the Griffin Hospital, Derby, Conn.; Physician, outpatient department, Yale-New Haven Hospital, New Haven, Conn.

Following the second operative procedure his clinical course was one of continued improvement, and on September 2nd he was discharged from the hospital with a T-tube in place.

On October 21st, after x-rays visualized a patient extrahepatic biliary system, the T-tube was removed. There was prompt healing of the wound, and on the last follow-up on November 11th he was back to a normal weight, eating well, and seeking gainful employment.

### Discussion

The current literature documents a rising incidence of systemic fungus infection over the past decade.<sup>2</sup> Various etiologic factors have been advanced to explain this phenomenon but the common denominator of a lowered resistance to infection and treatment with broad spectrum antibiotics is almost invariably present. This case documents the occurrence of a localized peritonitis without systemic infection due to *Candida albicans*. As pointed out by Dennis et al.,<sup>2</sup> a positive *Candida* culture should not necessarily be interpreted as a laboratory contaminant but should be interpreted as an ominous clinical finding. The presence of hyphae on a freshly stained smear, as in this case, can be a helpful adjunct to distinguish a virulent invasive infection from a laboratory contaminant.<sup>3</sup>

Once a diagnosis is established, the only currently available therapy is Amphotericin B. This drug is not without its side effects. In this particular patient shaking chills and fever invariably followed soon after the onset of infusion. Gastrointestinal symptoms have also been reported.<sup>4</sup> The dangerous nephrotoxic effects must be carefully watched for

and therapy may have to be discontinued. Andreole and Kravetz<sup>4</sup> report that BUN values of 20 to 30 mgs. per 100 ml. must not be exceeded if the renal damage is to remain in a reversible stage. Hypokalemia and anemia are also seen in patients on long term therapy.

Dosage schedule and adjustment are individualized. *Candida* is one of the most susceptible of the fungi to the effects of Amphotericin B, and long term therapy for an acute episode of Candidiasis is not required. The slow introduction of the agent and the gradual increasing of the dosage to a maximum level of 1 mg. per kilogram of body weight is important to minimize side effects. Premedication with promethazine and aspirin and the intravenous injection of 25 mg. of Solu Cortef with the onset of the infusion have helped to ameliorate the side effects of chills and fever.

### Conclusion

A case report of *Candida* peritonitis has been presented and its successful therapy with intravenous Amphotericin B has been discussed.

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"The cure of adenocarcinoma of the prostate is dependent upon us as physicians educating the public and our fellow physicians as to the simplicity and importance of regular periodic rectal exams. Without early recognition, the urologist's treatment is practically unchanged since the initial use of estrogens begun in the early 1940's." Charles Scott, Jr., M.D., Atlanta Georgia, "Carcinoma of the Prostate," *Journal of the Medical Association of Georgia*, 53: 278, 1964.



# THE PRESIDENT'S PAGE

## Conference Of Medical Society Presidents

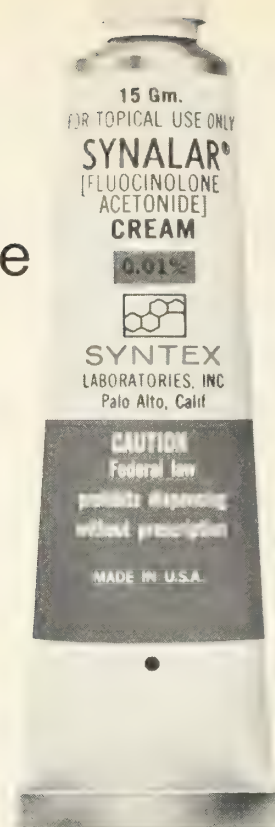
ON August 26-27th the Organization of State Medical Association Presidents met in Chicago to "discuss common problems, share experiences and help each other." Attendance is voluntary. Among members from 37 State Societies, Connecticut was represented by your President and E. Tremain Bradley, M.D. President-elect. The program included several topics of current interest and importance to the profession. Reports were heard concerning experience with Medicare (Title XVIII) in various parts of the nation. With few exceptions, hospitals have thus far been able to meet the increased demand for beds. Some hospitals have not participated due to inability to fulfill Civil Rights requirements. Direct billing is a widely accepted principle, however hospital based specialists are experiencing difficulties in reaching acceptable arrangements. It was generally felt that the Medicare program had not been in effect long enough to permit a meaningful evaluation.

Philip R. Lee, M.D., Assistant Secretary for Health and Scientific Affairs, U. S. Department of Health, Education and Welfare, speaking on the subject of Health Legislation in the 1960's, called attention to the vast number of medically oriented bills considered by the 88th and 89th Congresses. Noting that "momentous measures have been taken to meet the pressing national and community needs. 30 million Americans are living in poverty in urban and rural areas while metropolitan centers are plagued by over-crowding, obsolescence, segregation and a host of other ills—" he emphasized the significance of the 25 pieces of social legislation affecting the health of the American people passed by the 89th Congress. This government action involves mainly the allocation and distribution of funds for financing health care of segments of the population, provision of adequate facilities (hospitals, clinics, health centers, nursing homes) and for training of manpower (including nurses and allied personnel) necessary to implement the programs. Under Title XIX of the Medicare law twenty-five states have instituted programs to finance the costs of medical care of 3-52 per cent of their citizens. A plan adopted in New York State would cover total costs for 48 per cent of its residents. This plan had not yet met federal approval. Other federal funds are being made available under the Economic Opportunity Program for Project Head Start and the establishment of Neighborhood Health Centers. A new bill, S. 3009, now under consideration by Congress, would assist in financing hospital renewal projects and would encourage the development of group practice by making long-term mortgage financing available. Also under consideration by Congress is major legislation designed to strengthen the system of public health services. The Comprehensive Health Planning and Public Health Service Amendments of 1966 (S. 3008) would provide grants to states, beginning in fiscal 1968 with State Health officials distributing the funds, under an approved plan to meet the special health needs of their particular areas.

Dr. Hudson, American Medical Association President, has said "Medicare, as it now stands, is not an indigestible pill—the principal threat is not its provisions but the implications it perhaps carries for the future." It will become increasingly necessary for the profession to demonstrate the private sector's competence to carry out the technical, professional and administrative responsibilities which evolve upon it with clear indication to the public that no need exists for further government action.

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have an adverse effect on pregnancy, the safety of their use on pregnant females has not absolutely been established. Therefore, they should not be used extensively on pregnant patients, in large amounts, or for prolonged periods of time. 2. *Occlusive dressing method*—With occlusion of extensive areas, systemic absorption of the corticosteroid may occur, and suitable precautions should be taken. Occasional patients may show contact sensitivity to a particular dressing material or adhesive. Miliaria, folliculitis, or pyodermas have been seen infrequently with the use of this technique. The development of infection requires appropriate antibacterial therapy and discontinuation of the occlusive dressing method. Local atrophy and striae have been reported with protracted occlusive dressing therapy. While lesion relapses can be expected to occur in many psoriatic patients, remissions may persist for several weeks to several months in favorable cases. The patient whose psoriasis is in an active stage, with recent appearance of new lesions, may not be a good candidate and may show early relapse. Some plastic films may be flammable, and due care should be exercised in their use. Similarly, caution should be employed when such films are used on or left near children to avoid the possibility of accidental suffocation. **Side Effects:** Side effects are not ordinarily encountered with topically applied corticosteroids. As with all drugs, however, a few patients may react unfavorably to Synalar under certain conditions. **References:** 1. Cahn, M. M., and Levy, E. J.: *J New Drugs* 1:262 (Nov.-Dec.) 1961. 2. Meenan, F. O.: *J Irish Med Ass* 52:75 (Mar.) 1963. 3. Robinson, H. M., Jr., Raskin, J., and Dunseath, W. J. R.: *Southern Med J* 56:797 (Jul.) 1963.



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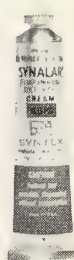
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## SUMMARY OF ACTIONS COUNCIL MEETING

**Wednesday, August 24, 1966**

### I. Attendance

Present in addition to the Chairman, Dr. S. J. Martin, were: Drs. Hess, Bradley, W. Martin, Goldberg, Brandon, H. Caplan, M. Caplan, Polivy, Grendon, Egan, Abbot, Spitz, Ayres, Cramer, Fabro, Grant, Petrie and Pelz. Also present: Mrs. Lindquist and Dr. Richards. Absent were: Drs. Gardner, Weise, Sr., Rogol, Hastings, Shepard, Nolan, Ciccarella, Wilson, Palomba and Roch.

### II. Routine Business

#### Approval Of Minutes

As printed and distributed, it was VOTED to approve the minutes of the meeting of July 14, 1966, with the following addition: That record be made of the Council's desire that future "minutes" of the CSMS and Connecticut General representatives' meetings on Part B of Medicare be reviewed and approved by the chairmen of both contingents before they are distributed as official.

#### Life Memberships

It was VOTED to approve applications for Life Membership received from the following eligible Active Members of the Society:

Irving H. Uvitsky, 3101 Main Street, Bridgeport (FCMA).

John R. Paul, 333 Cedar Street, New Haven (NHCMA)

John J. Gaffney, 215 Main Street, Danbury (FCMA)

#### Appointment—Committee On State Blood Bank

It was VOTED to appoint William L. Williams, Rockville, to membership on this Committee for the balance of the current year (to April, 1967).

### III. Old, New And Special Business

#### Communication—State Health Department

##### Re Tumor Registry

It was VOTED to accept, with thanks, the information provided by Henry Eisenberg, CSHD's Chief of the Chronic Disease Control Section, concerning follow-up procedure for cancer patients leaving and entering Connecticut. In brief, those leaving the State "are followed by the tumor registries of participating hospitals (in the new state of residence) whenever it is possible." When not pos-

sible, a request is sent "to (the new state's) Office of Vital Statistics requesting death certificate information." In reverse, this procedure is followed on patients moving into Connecticut, although sometimes they are not picked up until they register with a Connecticut hospital for follow-up and/or further therapy.

#### Report—Advisory Committee On Dependents Medical Care Program

It was VOTED to accept as information, and with commendation, the report filed by Robert R. Berneike, Chairman of the Advisory Committee on (Military) Dependents Medical Care Program, on a meeting held with representatives of ODMC to discuss implementation of the CSMS policy of reimbursing physicians on the basis of their "usual and customary fees, as determined at local level." In brief, the report indicated that the ODMC representatives had been receptive to implementing the policy in the Dependents Medical Care Program, and had promised to present to the Society for approval a new program which would embody the policy of "usual and customary fees" as far as possible within the limits imposed by Federal statutes. Meanwhile, to allow time to prepare and present such a new policy to the Society and for the Society to consider it for approval, it had been agreed to extend the present CSMS-ODMC agreement (which expires on September 30) for another six months.

#### Resolution Re Financial Arrangements Between Hospitals And Physicians

It was VOTED not to adopt a resolution on the financial arrangements between hospital administrations and hospital-based specialists, but to refer the resolution to a special ad hoc reference committee (to be appointed by the Chairman) for study and report to the Council, such report to extend the scope and intent of the resolution to all aspects of current and projected contractual financial arrangements for medical practice between hospital administrations and physicians in all branches of medicine. The Chairman appointed the special ad hoc committee as follows:

Sidney L. Cramer, Hartford, Chm. (Radiology)

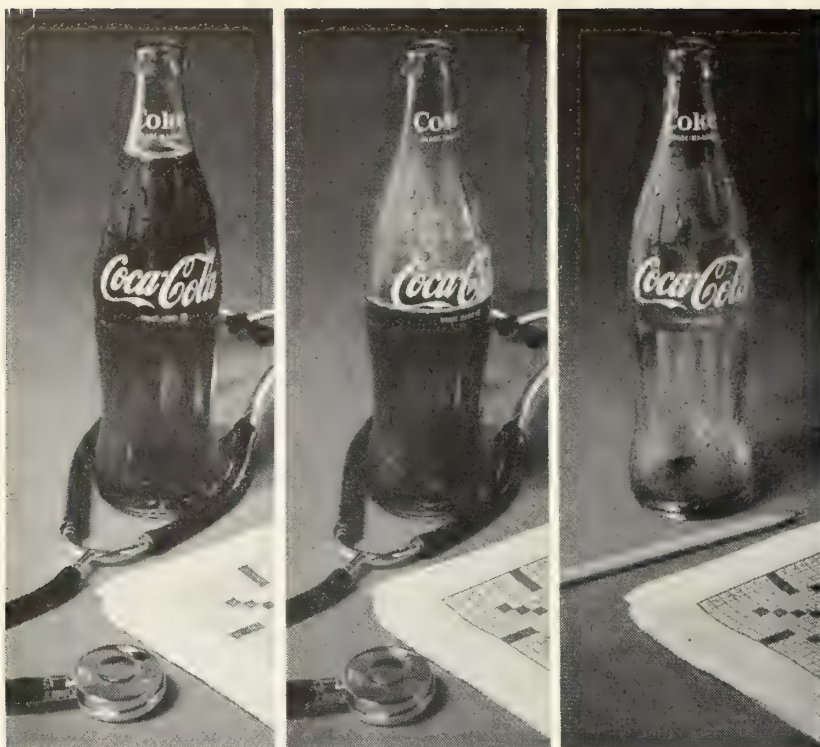
David A. Grendon, Sharon (Radiology)

John R. Egan, Old Saybrook (Medicine)

Benjamin Cohen, Hartford (Anesthesia)

Marcus S. Cox, Waterbury (Pathology)

John F. Nolan, Bridgeport (Surgery)



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**Report—Fiscal Advisory Committee To The Council**

Actions were taken on a report filed by the Fiscal Advisory Committee (presented by I. S. Goldberg, Treasurer) as follows:

1. *Membership in U.S. Chamber of Commerce*—It was VOTED to approve the recommendation of the FAC that the Society discontinue its membership in the U.S. Chamber, and *not* pay 1966-67 annual dues in the amount of \$600.
2. *Conference of County Medical Association Officers*—It was VOTED to approve the recommendation of the FAC that the Council authorize the holding of such a Conference (as outlined in a report submitted by the Ad Hoc Committee on Administrative Organization and Planning) and authorize the expenditure of up to \$650 to cover the costs attendant thereto.
3. *AMA-USPH Symposium on Immunizations*—It was VOTED to approve the recommendation of the FAC that the Council *not* appoint a member to represent the Society at this Symposium.
4. *Standby Authorization for publishing Connecticut M.D.*—It was VOTED to approve the recommendation of the FAC that the sum of \$700 be added to the General Manager's 1966 budget, to cover the costs of publishing two more issues of *Connecticut M.D.* during the current fiscal year, if such publication is directed or deemed to be desirable by the Council, the PR Division or the PR Director and General Manager jointly.
5. *Radio Series: "Your Health Today"* — It was VOTED to approve the recommendation of the FAC that the Council authorize the PR Division to implement a project to broadcast one-minute taped "health messages" over commercial radio stations in all county association areas (the tapes to be made by local physicians at convenient county-selected centers), and authorize the expenditure of up to \$720 in a twelve month period to share the production and distribution costs 50-50 with each participating county medical association, on the basis of the actual costs incurred by each such association.

**Recommendation—The Public Relations Division**

It was VOTED to approve a recommendation of the PR Division that the present two-committees under the Division be reduced to one committee of twenty-four members, and to refer the recommendation (with accompanying explanatory material) to the Subcommittee to Study and Revise the Bylaws for implementation (properly worded amendment) and report to the Council, for transmittal to the House of Delegates.

**Communication From CSMS Member**

**Re Welfare Drug Regulations**

Having reviewed a copy of a letter sent by a Toland County member to the State Welfare Department, in which the member protested against certain of the regulations covering the prescribing of drugs under the Medical Assistance Program, and also criticized the members of the Society's Advisory Committee to the State Commissioners of Welfare, Finance and Control for allegedly "approving" of such regulations, it was VOTED to: Inform the member (a) that his complaints re the drug regulations will be taken up with the Welfare Department through official channels, and (b) that the Council finds his criticisms of the Advisory Committee to be quite unwarranted, and strongly suggests that, in the future, the interests of the Society and its members will be best served if such criticisms of CSMS officials or committees are sent directly to the Council and *not* through an outside agency.

**Request For Information—Compensation Of Expert vs. Regular Medical Witness**

Having noted a statement in the 7/11/66 issue of AMA NEWS that: "At least one state (Connecticut) has adopted a rule that an "expert" physician witness may *not* be paid anything more than a "regular" witness fee (provided by law for any witness)", the Council VOTED to check on the veracity of this statement through legislative and/or legal counsel and, if confirmed, to refer the matter to the Committee on State Legislation for appropriate action to amend the Connecticut General Statutes in such a manner as will provide that an expert witness (in particular, a physician) may be paid a higher fee than a regular witness by the party who calls him to testify.

**Request For Information—Physician Liability In Chemical Tests For Intoxication**

Having noted a statement in the 7/25/66 issue of *Medical Economics* that only *two* states (New York and California) have passed laws protecting physicians against civil suit as a consequence of their having drawn blood samples (at the request of police officers) on persons arrested on suspicion of driving under the influence of alcohol, the Council VOTED to refer this statement to the Committee on State Legislation for study, report and recommendations concerning efforts to enact such a protective law in Connecticut.

N.B.: *The foregoing is a summary of the proceedings and actions of the Council on August 24, 1966. Detailed minutes of the meeting are on file at 160 St. Ronan Street, New Haven, for perusal by any interested member of the Society.*

**How long will  
it take her  
to recover from  
her hip fracture  
if she just  
doesn't care?**





**Does she really care?  
Is she alert, encouraged,  
positive and optimistic  
about getting completely  
well soon?**

**Or has she given in to  
the demoralizing impact  
of confinement, disability  
and dependency?**

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complicates convalescence,  
Alertonic can help...**

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\*Multiple of adult Minimum Daily Requirement supplied.

†The need for these substances in human nutrition has not been established.

**Indications:** 1. Functional fatigue such as that often associated with: a depressing life experience or stressful time of life; advancing years; convalescence; limited activity or confinement. 2. Poor appetite and vitamin-mineral deficiency as they occur in: patients having faulty eating habits; geriatric patients who are losing interest in food; patients convalescing from debilitating illness or surgery.

**Dosage:** Adults, 1 tablespoonful; children (over 15 years old), 1 to 2 teaspoonfuls; children (4 to 15 years old), 1 teaspoonful. To be taken three times daily 30 minutes before meals.

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**ANESTHESIOLOGIST**—40 years of age, Board eligible, Connecticut license. Military obligations completed, would like to associate with another physician or practice in an institution.

**INTERNIST**—29 years of age, married, Board eligible. Would like to practice in either a solo or partnership situation within easy traveling distance of New York.

**PEDIATRICIAN**—37 year old Board eligible pediatrician with background in general pediatrics and pediatric oncology desires to associate with other pediatricians in New Haven area. Military obligations completed, applied for Connecticut license.

## PLACEMENT OPPORTUNITIES

**PSYCHIATRIST** needed for a community-oriented mental hospital, to direct service within a 2300-bed State mental hospital. Opportunity for teaching, clinical work and research. Has to develop and direct team of social workers, psychiatric residents, psychologists and more than 80 nursing staff personnel. O.P.D., day care, in-patient consultation and emergency care available. Opportunity for association with Wesleyan, Yale and University of Conn. Salary: \$14,240-\$20,000, depending on qualifications and experience. Excellent fringe benefits and annual leave to attend medical conventions. All particulars should be in first letter, including references. Apply—John F. Lowney, Jr., M.D., Supt., Connecticut Valley Hospital, Box 351, Middletown, Conn. 06458.

**PATHOLOGIST**—full-time or half-time to direct clinical laboratory in 2300-bed mental hospital. Ample opportunity for research and teaching available. Well equipped and staffed laboratory, emphasis on neuropathology. Board certified or eligible pathologist preferred. Salary: \$14,740-\$19,000. Excellent fringe benefits. All particulars and references should be sent in first letter. Contact—John F. Lowney, Jr., M.D., Supt., Connecticut Valley Hospital, Box 351, Middletown, Conn. 06458.

**CLINICAL DIRECTOR** to develop program in psychiatric hospital with emphasis on psychosomatic medicine. Opportunity for experience in employees' health clinic, workmen's compensation, clinic and psychopharmacologic drug research. Will direct department staffed with 7 physicians. EEG, EKG, Radiology, Ophthalmology Depts. already fully equipped and staffed. Consultants available in all medical and psychiatric specialties.

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G.P. to specialize in psychiatry. Psychiatric residencies available in community-oriented mental hospital. Associated with Yale Depts. of Psychiatry and Neurology. Opportunities for training in areas of special interest. Arrangements can be made to be accepted for degrees in community mental health and hospital administration at Yale. Psychoanalytic training available at Western New England Psychoanalytic Institute. Salary \$12,000 annually under NIMH grant. Excellent fringe benefits. All particulars and references included in first letter. Contact—John F. Lowney, Jr., M.D., Supt., Connecticut Valley Hospital, Box 351, Middletown, Conn. 06458. An Equal Opportunity Employer.

**CLINICAL PHARMACOLOGIST** — Physician who wants to combine medical knowledge, scientific inquisitiveness and administrative skills. Highly desirable are previous experience in pharmaceutical industry, background of private practice and some type of specialized medical training, although a strength in one area may outweigh a lack in the others. As a member of the Research Div., he will be active in the planning of new medicinal research programs. Between 10% and 20% of the time, the physician will be on scientific field trips or attending various professional meetings, but will rarely be gone for more than three consecutive days. Members of the Clinical Pharmacology Dept. are encouraged to publish scientific papers based on their own studies. Contact: D. V. Vines, Personnel Mgr., Chas. Pfizer & Co., Inc., Groton, Conn., 06340.

**INTERNIST**—The Chapel Medical Group in New Haven is looking for an internist. This is a three-man group and they have a regularly visiting specialist consultant staff with modern clinic facilities, with scheduled training and vacation periods. The starting salary is \$15,000-\$18,000 with a partnership in one year. If you are interested, please submit qualifications to 1308 Chapel Street, New Haven, Connecticut 06511.

ANYONE INTERESTED IN THE ABOVE IS ASKED TO CONTACT THE GENERAL MANAGER'S OFFICE, 160 ST. RONAN STREET, NEW HAVEN, CONN. 06511.



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**(allobarbitol and acetaminophen CIBA)**

**Indications:** For relief of pain and discomfort of simple headache; neuralgia, myalgia, and musculoskeletal pain; dysmenorrhea; bursitis; sinusitis; fibrositis. Also indicated to reduce fever and to relieve discomfort due to respiratory infections, influenza, and other febrile conditions.

**Contraindication:** Not recommended during pregnancy.

**Caution:** May be habit-forming. Do not use in patients sensitive to barbiturates or in those with moderate to severe hepatic disease.

**Side Effects:** Nausea, transitory dizziness, rash. Overdosage of allobarbitol produces symptoms typical of acute barbiturate excess.

**Dosage:** *Adults:* 1 or 2 tablets every 4 hours. Not to exceed 8 tablets in 24 hours. *Children 6 to 12:* 1/2 to 1 tablet every 4 hours. Not to exceed 4 tablets in 24 hours.

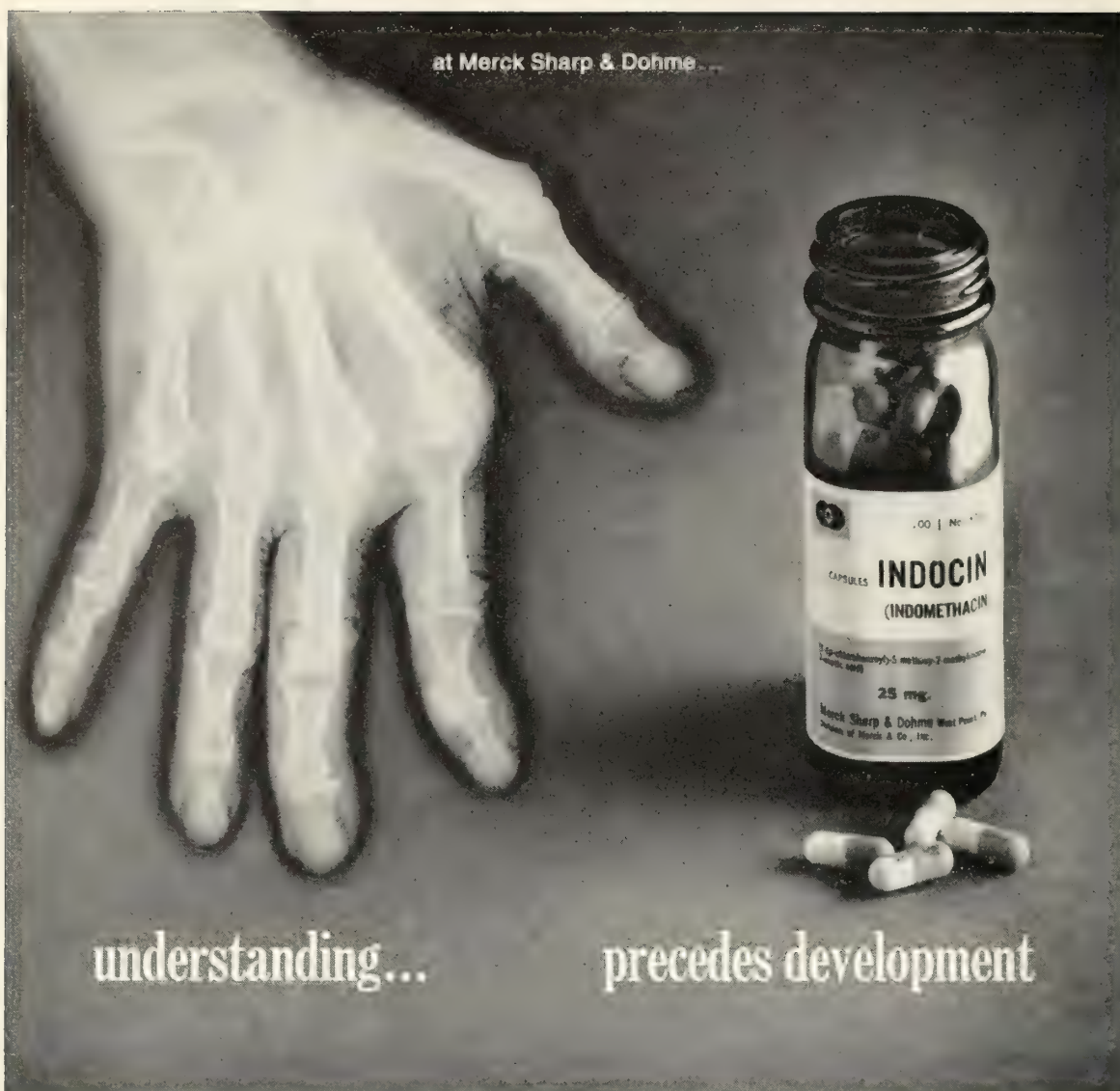
**Supplied:** *Tablets* (white, scored), each containing 15 mg allobarbitol and 300 mg acetaminophen; units of 3 bottles of 30.

**For your convenience — prescription-size bottle of 30.**

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## INDOMETHACIN

**Indications:** Chronic and acute rheumatoid arthritis, rheumatoid (ankylosing) spondylitis, degenerative joint disease (osteoarthritis) of the hip, and gout.

**Contraindications:** Active peptic ulcer, gastritis, regional enteritis, or ulcerative colitis. Safety in pregnancy has not been established. Not recommended for pediatric age groups.

**Warning:** Patients who experience dizziness, lightheadedness, or feelings of detachment on INDOCIN should be cautioned against operating motor vehicles, machinery, climbing ladders, etc. Use cautiously in patients with psychiatric disturbances, epilepsy, or parkinsonism.

**Precautions and Adverse Reactions:** Most commonly, headache, dizziness, lightheadedness, G.I. disturbances. The C.N.S. effects are often transient and frequently disappear with continued treatment or reduced dosage. The severity of these effects may occasionally require cessation of therapy. G.I. effects may be minimized by giving the drug with food or with antacids or immediately after meals. Ulceration of the stomach, duodenum, or small intestine has been reported and, in a few instances, severe bleeding with perforation and death. Gastrointestinal bleeding with no obvious ulcer formation has also been noted; INDOCIN should be discontinued if G.I. bleeding occurs. As a result of G.I. bleeding, some patients may manifest anemia, and for this reason periodic hemoglobin determinations are recommended. Rare reports of effects not definitely known to be attributable to INDOCIN include bleeding from the sigmoid colon (either from a diverticulum or without a known previous pathologic condition), perforation of preexisting sigmoid lesions (diverticulum, carcinoma), and hematuria. In other rare cases, a diagnosis of gastritis has been made while the drug was being given. One patient developed ulcerative colitis, and another, regional ileitis, while receiving INDOCIN; when the drug was given to patients with preexisting ulcerative colitis, there was an increase in abdominal pain. Infrequently observed side effects may include drowsiness, tinnitus, mental confusion, depression and other psychic disturbances, blurred vision, stomatitis, pruritus, edema, and hypersensitivity reactions. Slight BUN elevation, usually transient, has been seen in some patients, although the preponderance of evidence indicates that INDOCIN does not adversely affect renal function, even in patients with preexisting renal disease. Nevertheless, renal function should be checked periodically in patients on long-term therapy. Leukopenia has been seen in a few patients. Transient elevations in alkaline phosphatase, cephalin-cholesterol flocculation, and thymol turbidity tests have been observed in some patients and, rarely, elevations of SGOT values; the relationship of these changes to the drug, if any, has not been established. As with any new drug, patients should be followed carefully to detect unusual manifestations of drug sensitivity. Before prescribing or administering, read product circular with package or available on request.

## Many Football Knee Injuries Preventable

The prevention of knee injuries in football should rate priority attention, even though protecting the knee is difficult.

A joint statement by the National Federation of State High School Athletic Associations and the American Medical Association's Committee on the Medical Aspects of Sports offers suggestions for greater player protection.

The best protection, the statement said, may be the player's own efforts to build strength in leg muscles supporting the knee. These are the knee's only supporting structures whose strength can be improved.

It is a paradox that the knee—considered one of the strongest joints in the body—is the most commonly injured major point in contact sports, the statement noted. This is partly due to the knee's unusual structure. It is more than a mere hinge; the leg must rotate as the joint hinges.

This versatile joint movement makes possible the crowd-thrilling action of a dodging, weaving football "scat back." On the other hand, the complexity of the knee's structure also makes the player vulnerable to disabling injury.

Bad practices cause many knee injuries, the statement said, and such practices can only be eliminated by better coaching and strict control of the game. These practices include clipping, blind-side blocking, piling-on after tackles, and unnecessary contact after an official's whistle has sounded.

Knee pads help avoid bruise-type injuries, but protective equipment otherwise offers primarily only psychological benefits, the statement said.

The player can help prevent injury by following his coach's advice to shorten and quicken his stride when in the zone of action. This lessens the time a foot is on the ground—the only time a knee injury can occur.

Some football shoes now have cleatless heels, an effort to prevent knee injury by giving the foot more freedom of movement. Results to date are encouraging, but continued study is recommended to learn more specifically the relative advantages of cleatless heels, the statement said.

If it were possible, the best way to prevent knee injury would be to select only athletes who were bowlegged and pigeon-toed, the statement noted. These leg alignments permit the least possible stress on the knee.

Beyond such an impractical solution, the best protection remains adherence to good practices, strict rule enforcement, and building-up of strength in the thigh, hamstring, and calf-muscles.

### 1966 MEETINGS

**October 27** — 183rd Semi-Annual Meeting of New Haven County Medical Association to be held at Waverly Inn, Cheshire, Connecticut at 3:30 P.M.

### 1967 MEETINGS

**January 17-19** — New England Postgraduate Assembly will be held at the Statler Hilton Hotel, Boston, Massachusetts. Advance Program will be sent in early December.

**April 12-13** — Seminar on Hospital Infections in Connecticut to be sponsored jointly by the Connecticut State Medical Society, Connecticut Hospital Association, Yale University School of Medicine, the Connecticut State Department of Health and the Communicable Disease Center of the Public Health Service.

**April 25-27** — 175th Annual Meeting of the Connecticut State Medical Society to be held at the Statler-Hilton Hotel, Hartford, Connecticut.

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### 1966 COUNTY SEMI-ANNUAL MEETINGS

|                   |           |                    |
|-------------------|-----------|--------------------|
| FAIRFIELD COUNTY  | WEDNESDAY | OCTOBER 5, 1966    |
| HARTFORD COUNTY   | WEDNESDAY | SEPTEMBER 21, 1966 |
| LITCHFIELD COUNTY | TUESDAY   | OCTOBER 11, 1966   |
| MIDDLESEX COUNTY  | THURSDAY  | OCTOBER 13, 1966   |
| NEW HAVEN COUNTY  | THURSDAY  | OCTOBER 27, 1966   |
| NEW LONDON COUNTY | THURSDAY  | OCTOBER 6, 1966    |
| TOLLAND COUNTY    | TUESDAY   | OCTOBER 18, 1966   |
| WINDHAM COUNTY    | THURSDAY  | OCTOBER 20, 1966   |



# Experts, Enclaves, And The Public Interest

**John H. Knowles, M.D.\***

■ We are a nation of experts and technical specialists. The vast expansion of higher education in this country is the answer to society's demands for more well-trained specialists, rather than a recognition of the inherent values of education. The validity of the role of the generalist, or non-expert, is steadily denied by the purveyors of specialized knowledge. "A little knowledge is a bad thing" is deeply ingrained in our culture and as Barzun has said, "Every subject today confronts the tyranny of the professional" and "we face an endless separatism based on loyalty to the parish pump and linked with the unanimous desire to obliterate the mere observer by denying the validity of his role."<sup>1</sup>

The role of the administrator becomes more central and crucial in such a society—and the importance of his role is matched by increasing defiance of his responsibility and authority. The University President can be sent packing by the collective action of irate students. The authority of the Courts is challenged and ridiculed by New York City transit workers. The Condon-Wadlin Act is flaunted and, instead of being enforced, is changed by beleaguered politicians and judges to fit the season of discontent. The new found power of collective action, whether it be by unions of students, Cape Kennedy technicians, transit workers, nurses, physicians or radiologists, or Civil Rights sympathizers is everywhere challenging the validity and uncertain virtues of established systems and organizational power structures. Does this represent the new revolt of the masses, and as John Adams warned, the main weakness of a democracy, i.e., the tyranny of the unenlightened majority? Or, does it represent the revolt of the non-expert masses against the inadequate leadership of those experts and specialists presently occupying the seats of power and decision making? I suggest that it is just as much the latter as it might popularly be thought to be the former.

The new powers of expanding forms of communication point the finger squarely at the experts. It would appear that they have failed in public education and that this failure represents a lack of

moral commitment outside their own areas of expertise. It is also a failure of those who control the forms of communication, sacrificing accuracy to sensationalism, and downgrading the human spirit by purveying the seamy, beastly side of life to the inevitable exclusion of rational discussion of major issues. The reporting of those events which uplift the spirit, increase the understanding and quicken the ethical sense of a harassed and nervous citizenry are left to a handful of newspapers and to the off-beat "intellectual rags."

The future of a democracy depends on the ability of an enlightened citizenry to make viable choices. But choices are not being made and active participation by an understanding public in the major issues of the day has succumbed to apathy, alienation, and a lateral drift which favors and looks to central authority for the solution of problems.

Hans Morganthau puts it well when he says, ". . . our age has witnessed a drastic shift in power from the people at large to the government from the legislative to the executive branch, and within the executive branch from the democratically responsible officials to certain technological elites. These shifts of power are the result of the revolutions in the technologies of transportation, communication, and warfare. These revolutions have transformed the business of government into an esoteric undertaking, unintelligible to the uninitiated and far removed from the experience of the man in the street. The issues of whether or not to build an anti-missile system or fallout shelters are different in quality from say, the issue of the prohibition of child labor of more than half a century ago. In contrast to the former, the latter was intelligible to the man in the street, and he was capable of passing moral judgement on it and translating the judgment into political action. In consequence, political participation has given way to apathy, and 'consensus' has taken the place of political controversy."<sup>2</sup>

*Presented at the annual meeting of the Connecticut Hospital Association, at the New Haven Lawn Club, New Haven, Connecticut, June 9, 1966.*

DR. JOHN H. KNOWLES, General Director, Massachusetts General Hospital, Boston, Mass.

There has also been a revolution in the technology of medicine—and the physician (and his collective self, the American Medical Association) who understands and purveys the technology has occupied the position of expert-specialist beautifully. And, like all experts, he is extremely valuable while also being extremely troublesome.

### The Expert

There is an old saying that the expert should always be on tap but never on top. Harold Laski stated it so when he said

"... expertise ... sacrifices the insight of common sense to intensity of experience ... Intensity of vision destroys the sense of proportion ... the knowledge of what can be done with the results obtained in special disciplines seems to require a type of coordinating mind to which the expert as such is simply irrelevant ... it is only the juxtaposition of the statesman between the expert and the public which makes specialist conclusions capable of application ... that indeed is the statesman's basic task. He represents at his best supreme common sense in relation to expertise."<sup>3</sup>

The expert physician is a specialist and we are glad to have him help us when we are sick in an area of our body that corresponds to his specialty. For this reason, I would agree with President Pusey of Harvard who believes that we need more, not fewer, experts—for the specialist is the one who can solve our special problems requiring expertise, be they medical, legal, social, architectural or what have you. I agree completely.

We fall into trouble with the expert-specialist however for two reasons:—1) he *can* function and get along quite well without moral commitment outside his own area of expertise; and 2) he has the perfectly human desire to dominate outside his own area of expertise, and will recognize no limitations to his charismatic authority. Ortega y Gasset has said—

"We shall have to say that he is a learned ignoramus, which is a very serious matter, as it implies that he is a person who is ignorant, not in the fashion of the ignorant man, but with all the petulance of one who is learned in his own special line.

"And such in fact is the behavior of the specialist. In politics, in art, in social usages, in the other sciences, he will adopt the attitude of primitive, ignorant man; but he will adopt them forcefully and with self-sufficiency, and will not admit of—this is the paradox—specialists in those matters. By specializing him, civilization has made him hermetic and self-satisfied within his limitations; but this very inner feeling of dominance and worth will induce him to wish to pre-

dominate outside his specialty.\* The result is that even in this case, representing a maximum of qualification in man—specialization—and therefore the thing most opposed to the mass-man, the result is that he will behave in almost all spheres of life as does the unqualified, the mass-man.

"This is no mere wild statement. Anyone who wishes can observe the stupidity of thought, judgment, and action shown today in politics, art, religion, and the general problems of life and the world by the 'men of science', and of course, behind them, the doctors, engineers, financiers, teachers, and so on. That state of 'not listening', of not submitting to higher courts of appeal which I have repeatedly put forward as characteristic of the mass-man, reaches its height precisely in these partially qualified men. They symbolize, and to a great extent constitute, the actual dominion of the masses. . . ."<sup>4</sup>

The expert-specialist position of learned ignominious, coupled with his capacity to get along without any necessary moral commitment outside his own area lies at the very roots of the modern doctor's dilemma. The roots can be traced back to his premedical and medical education which have successfully forced his attention on medicine *only* as a biological science to its exclusion as a social science.

First of all, one should turn one's attention to the premedical student. Once he has declared himself, two forces are set in motion, neither of which is entirely desirable. The first is acceleration of the curriculum, and the second is an "overwhelming obsession for science," so that his interests are constricted and restricted, and the liberal arts are not given the full measure of attention. What emerges from college may thus be an incomplete product, politically and socially naive, and not optimally prepared to be, as Lionel Trilling has said, "at home in and in control of the modern world, . . . the true purpose of all study." President Pusey, of Harvard, has said:

"The humanities have a very special place in a university, especially perhaps because of the pleasure they give, but also because of the heightened effects which experience of them can produce in individuals in terms of enlivened imagination, increased responsiveness, broadened interest, clarified purpose and in the end also, quickened ethical sense."

\* The modern example is the expert stance that the physician (and the A.M.A.) assumes in relation to the social and economic problems of medical care—subjects about which the average physician knows almost nothing, but speaks with great authority. This defect is compounded by economic self-interest which gives a certain unfortunate slant to the pronouncements made by our overextended expert.



The medical school curriculum accelerates the constricting effect of the student's premedical education by its complete emphasis on a foundation of basic science in the first two years of medical school. The opportunity still exists to introduce the liberal arts, humanities, and social sciences of medicine, but it is not seized. This history of medicine—its people, its institutions and its social setting — is neglected, as the politics and the economics of medicine are. The student is relentlessly forced to focus on the individual doctor-patient relation as an object, and his own subjective self-understanding and his understanding of the world around him flags.

At the end of his four years, he is a highly individualistic person, trained to take immediate action with the individual patient and to expect immediate rewards, with his knowledge firmly grounded in science. The primary purpose of medical education—that is, to understand disease and to be able to manage sick people—has been fulfilled, but the broader issue of the physician's place and problems in the world at large has been neglected. The world of the health profession and its institutions has been left undescribed and unstudied.

The roots of our dilemma with the expert-specialist physician can be traced further back to the origins of human social behaviour and particularly that characterizing a profession—and that is that the members of any profession have a self-protective or guild function and look inward as well as a service and public responsibility, in which case they look outward. Today, the medical profession is looking inward and watching outward—watching out for what a high official of the A.M.A. has termed the three main enemies of the profession — the Universities, the hospitals and the Federal Government. The medical profession is the avowed enemy of any bureaucracy, particularly when they have little control of it themselves.

### Enclaves

The word enclave comes from the French and means, literally, "nailed in". It refers to "a piece of territory entirely shut in by foreign dominions". Our military advisers have debated the desirability of establishing coastal enclaves in Vietnam. Our enclave becomes the exclave of the Vietnamese, i.e., that piece of territory isolated from the home country by a foreign power.

I labor these terms for I wish to draw an analogy and try to establish a concept. The American hospital today has become a focal point of medical care—even the doctor's office is in or adjacent to the local hospital today and for obvious reasons which I will not repeat. The hospital has emerged from a passive receptacle for the indigent sick in

the 19th century to the modern health center for all social and economic classes. It is an organized, social instrument consisting of the grouping of health professionals, employees and administrators, and of the massive and expensive technology of medical care all under one roof, or in adjacent buildings.

Is it, indeed, what it should be, a smoothly working, highly efficient organization? The answer is no and for many reasons:

1. the impossibility of timing and scheduling illness, as well as the doctor's valuable time;
2. inadequate manpower and inadequate training programs for that limited manpower;
3. the necessity to run a 24 hour, 7 day a week operation for unforeseen and uneven demands;
4. an incredible lack of and indeed, resistance to planning, characteristic of the medical profession, and so on.

But another and increasingly important reason is the establishment of *enclaves* in the hospital by nationally (and locally) organized groups of experts—all busily carving out their areas of expertise, their enclaves if you will—all functioning in isolated fashion without any necessary moral commitment outside their own territory—or what to me is an exclave in my hospital.

I refer to

1. the specialty Boards and the Council on Medical Education of the A.M.A.—who control the length and breadth of our in-hospital graduate residency programs—and steadily expand the requirements for specialists in the face of a shortage of physicians—partly due to lack of moral commitment outside of their immediate responsibility for standard setting and partly due to the effects of syndicalism;

2. the National League for Nursing which, in the face of a shortage of nurses is actively fighting the hospital diploma schools which provide the country presently with three-quarters of our nurse supply;

3. the American Colleges of Radiology, Pathology and Anesthesiology hell-bent on getting out from under the hospital organization and salaried arrangements and successfully disrupting through the Medicare Law a system which had been highly successful in protecting patient, doctor and hospital from exploitation;

4. the medical schools who have used their hospitals for teaching and research and neglected the service and community needs by overemphasis on the university function;

5. State Welfare Departments who, through emphasizing savings for the taxpayer by shortsighted underpayment of hospitals, have effectively

choked the development and even maintenance of our large urban hospitals—and many more examples which would include the Blue Cross, the Joint Commission on Accreditation, the A.H.A., the American College of Surgeons and so on.

### The Public Interest

With our experts and our enclaves, what has happened to the public interest—the organization, distribution, availability, utilization, quality and financing of health services and facilities? We have, I believe, muddled through fairly well and I am not a pessimist or a cynic but

1. the cost of medical care continues to skyrocket;

2. our hospital and other health facilities are in sad repair and will become increasingly inadequate to the task;

3. there is a drastic shortage of health manpower—doctors, nurses, technicians and so on—as well as a shortage of nursing home and hospital beds; and

4. there is little if any true regional planning to improve health services and avoid reduplication.

Our experts continue on their enclaves without apparent concern. I have many times stated to my medical colleagues that I am unalterably opposed to the expansion of central (Federal) authority—that the hazards of the Welfare State—a supine citizenry, an over-weening bureaucracy, and an erosion of individual initiative—must be avoided at all costs—and that a private system of medicine carried out in *voluntary* hospitals, supported and shaped by the local community who need and want the best health services has never been exceeded by any Government program—at least in this Country. I urge them to get together, consider the remaining problems (after Medicare), and act in a socially responsible fashion for there can be little freedom without responsibility. I ask the enclave leaders to consider the larger issues while they fight for their vested interests.

Meanwhile, the public knows of the problems of rising costs, manpower shortages, and inadequate hospital and nursing home facilities and hears one of two things from the experts and the enclave—

1. *“that’s not our business—we’ll serve our expert function and somebody else will have to do something about the other and larger problems”* or

2. *“there are no problems”*—which statement is continually given in authoritarian tones by our idiot savants (or learned ignoramous). Perhaps we should say with Pogo that “We have met the enemy and they are us!”

With the advent of Medicare, several crucial changes will occur, the most important of which are that

1. Public scrutiny of hospital costs and doctor’s fees will increase;

2. Equitable rates of reimbursement will be forced on State Welfare Departments, which will have to be uniform with rates paid by the Federal Government under Title 18;

3. Utilization of doctors and hospitals will increase, and with it, increased demands for better utilization of hospital beds—in this regard the requirement of a Utilization Committee is a most important and necessary change in hospital practice (necessitated by Medicare);

4. After-caring facilities will be shown to be grossly inadequate;

5. Hospital facilities will be strained and the need for new capital expenditures will become acute;

6. Manpower shortages will be accentuated;

7. Medical school-teaching hospital relationships will be altered and clinical teaching will change;

8. The relation of radiologists etc. to the hospital and the medical school will change and the manpower shortage here will become more acute;

9. Costs will increase markedly in both hospitals (Medicare tax, minimum wage, collective bargaining, etc.) and in doctors fees (Plan B inflation!);

10. The public and our local and national political leaders will demand and ultimately force regional planning and control;

11. Our capacity to strike new organizational arrangements within medicine and hospitals and to participate in the political arena will test us drastically and it is in these areas that I believe we have our greatest problems and greatest opportunity. Our political leaders are deeply concerned at this very moment that we in the medical world will not be able to fulfill the new expectations of the public as a consequence of Medicare. Will they help us or will they put the blame on us and use us as their scapegoats?

We must, I believe, develop new organizational arrangements and new methods of communicating with the public—arrangements which will recognize the central position of the expert and yet be able to articulate his work effectively with the public interest. The public interest must be based on reliable information and knowledge in depth, or apathy and consensus will rule the day, and our political leaders will drift laterally.

An example of a new organizational arrangement can be related to the present structure of the national association of hospitals called the American Hospital Association. In its present form it is essentially a group of hospital administrators who meet to discuss the problems of hospitals generally, but who at the moment do not enjoy effective working



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**Side Effects:** Overstimulation of the central nervous system, jitteriness and insomnia or drowsiness.

Dextro-amphetamine sulfate: Insomnia, excitability, and increased motor activity are common and ordinarily mild side effects. Confusion, anxiety, aggressiveness, increased libido, and hallucinations have also been observed, especially in mentally ill patients. Rebound fatigue and depression may follow central stimulation. Other effects may include dry mouth, anorexia, nausea, vomiting, diarrhea, and increased cardiovascular reactivity.

Meprobamate: Drowsiness may occur and can be associated with ataxia; the symptom can usually be controlled by decreasing the dose, or by concomitant administration of central stimulants. Allergic or idiosyncratic reactions: maculopapular rash, acute nonthrombocytopenic purpura with petechiae, ecchymoses, peripheral edema and fever, transient leukopenia. A case of fatal bullous dermatitis, following administration of meprobamate and prednisolone, has been reported. Hypersensitivity has produced fever, fainting spells, angioneurotic edema, bronchial spasms, hypotensive crises (1 fatal case), anuria, stomatitis, proctitis (1 case), anaphylaxis, agranulocytosis and thrombocytopenic purpura, and a fatal instance of aplastic anemia, but only when other drugs known to elicit these conditions were given concomitantly. Fast EEG activity, usually after excessive dosage. Impairment of visual accommodation. Massive overdosage may produce drowsiness lethargy, stupor, ataxia, coma, shock, vasomotor and respiratory collapse.



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relationships with other powerful groups or enclave leaders, if you will, which are essentially shaping and directing the American hospital today. Would it be a reasonable idea to restructure the American Hospital Association and organize it on the basis of a well organized hospital with hospital trustees in the ultimate position of authority, hospital directors as the executive directors of the Association and then medical staff, nursing staff and so on grouped organizationally within the national association as they are in a well managed hospital. In this way outside power groups could play the same role in the national organization that they enjoy in their own hospitals today. With the best representatives of all these various special interests working together, one might hope for better articulation of hospital interests with the public interest at large. The final authority would be the lay board of Trustees who articulate the private hospital interest with the public interest generally. At the moment the hospital administrators meet and although they have functioned well in the national Association, there is the constant hazard of assuming an expert stance and looking inward as a guild would rather than outward.

Certainly for the future there must be coordination and integration of public and private interests to provide health services of high quality which neither a public or a private system has been able or willing to do alone. We are entering into a new era of so-called "creative federalism" in which central Government is dedicated to problem solving by pumping large amounts of money into regions hoping that local politicians can evolve new systems to use the money wisely on a regional basis. Federalism can be creative only if an enlightened citizenry is willing to exercise maximal responsibility on a regional basis. The new Heart Disease, Cancer and Stroke Law represents an example of creative federalism. The question remains whether the local community of physicians and other interested parties can seize the opportunity to create better health services. In this regard I firmly believe that the hospital, its staff, employees, administration and trustees represent a politically viable unit of planning.

Perhaps it is time the medical profession developed what Max Weber called the three cardinal qualities of the politician, namely a feeling of responsibility, a sense of proportion and finally, passion. In the latter instance I mean passionate

commitment to the solution of public problems in medical care and not passionate commitment to one's guild or one's own expert interest.

The time is ripe for new moral commitment and action in the public interest for as Dante said—"The hottest places in Hell are reserved for those who, in a period of moral crisis, maintain their neutrality."

I would like to state most emphatically once again that I am proud to be a doctor and to be a member of the medical profession in the United States. I am a member of both the Massachusetts Medical Society and the American Medical Association and I have tried to work within the ranks of organized medicine to achieve goals which I find are totally shared by my colleagues. At the same time I find myself at odds with organized medicine as to how best to achieve these goals. I can assure you that if the present activities of organized medicine persist, the day will not be too far off when voluntary hospitals and private practice of medicine are taken over completely by the U.S. Government. If we fail to solve obvious problems on a local, private basis, then indeed the federal government should take us over in the public interest.

I should also say that the problems that apply to medicine and the public interest can just as well apply to other professional groups or special interests, such as the law, the ministry, the political system, the business world and so on. Perhaps this polemic is a broad indictment of our present American culture, its values and its attitudes. It is also a plea for new forms of moral commitment and organizational arrangements, so that a highly specialized country can move forward.

In conclusion I am reminded of the statement of J. Mason Brown who said—"Existence is a strange bargain. Life owes us little; we owe it everything. The only true happiness comes from squandering ourselves for a purpose."

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# WOMAN'S AUXILIARY

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L-R: Mrs. William R. Richards, Mrs. Jacques H. Green, Mrs. John Mendillo

## Nightmare Doll House

A strange sounding title for a project in which the Connecticut State Medical Society and its Woman's Auxiliary cooperated! This Doll House exhibit was a Community Service project originally thought up by the Woman's Auxiliary to the Hawaiian Medical Society. Our women were intrigued by it and decided they would like to try it with the cooperation of our Medical Society. Since there was comparatively little time to plan, research, and execute the idea between June and the end of August, the Woman's Auxiliary to the New Haven County Medical Association accepted the idea at their first Board Meeting and proceeded with the plans. The result was a beautifully detailed, inexpensive, ranch style, easy-to-view home, filled with 37 commonly seen Safety Hazards.

We sincerely hope that all the members of the Medical Society and the Auxiliary will have an opportunity to view this exhibit. All the women who gave their time to "sit" with it at the North Haven Fair said they enjoyed the experience in spite of the physical discomforts involved, such as

the heat, the cold at night, the late hours (to 11:00 P.M.), and the increasingly pungent odors of the prize vegetables surrounding them (after exposure of four days).

The interested groups of spectators included families who were brought back to the doll house after younger children had seen it and wanted to show their parents what they had learned; children in groups who discussed having learned about some of the hazards in the classroom; adults whose comments were: "Isn't it a mess? Just like ours sometimes." "Look at that woman smoking in bed, I'm always telling you not to do that!" "Look at all that cleaning stuff under the sink—see what happens—the kids get after it and get poisoned!" "That woman on the table—I'm always doing that—standing on a box—only I usually stand on a chair—just as bad!" Adults do not seem to have been as aware of the dangers of reaching for an electric appliance from the tub as children were. The children also noticed the overloaded circuit in the living room more quickly than the adults.

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## OBITUARIES

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### **Ernest H. Ferrell, Jr., M.D.**

**1923-1966**

After two and one half years of declining health, the courageous battle came to an end for Dr. Ernest Ferrell on July 13th, 1966. This unrelenting struggle for health attests to his noble spirit since, as a physician, he could not be spared the full knowledge of the nature of his illness. He continued with this bravely without self pity and served as an inspiration to those around him.

Dr. Ferrell was born in Cleveland, Ohio on November 25th, 1923, son of Ernest and Edna Rentsch Ferrell. He loved sports, and was especially interested in scouting. His parents moved to Waterville, Ohio where he graduated from High School. Early in life he had a desire to become a doctor of medicine. He received a Bachelor of Science degree from Bowling Green College. He was a graduate of Western Reserve University Medical School, and interned at Grace New Haven Hospital, where he was also a surgical resident. He spent two years as a Navy physician. He was a fellow of the American College of Surgeons; American Medical Association; New Haven County Medical Association and New Haven Medical Society; Connecticut State Medical Society. He is also a member of the Woodbridge Club. Dr. Ferrell is survived by his four sons: Thomas, William, James and Jeffery, and by his wife Florence. It may truly be said that no patient has ever received more efficient, attentive, cheerful and loving care than that given by his nurse and wife Florence.

We will all remember and cherish him for his warmth of personality and compassion for the ill. Because of the desire to help perpetuate the memory of our beloved colleague, his father, Mr. Ernest H. Ferrell, Sr., prepared a memorial pamphlet in his son's honor. I have taken the liberty of borrowing freely from the memorial pamphlet.

It seems most fitting that a tribute to his memory be concluded by a direct quotation from this pamphlet, which I shall now add.

"It has been said that a man who lives in the minds of his contemporaries, has built his own monument. Such a person has built a greater monument than any carved stone."

STEWART J. PETRIE, M.D.

### **Harry S. Reynolds, M.D.**

**1888 - 1966**

Dr. Harry S. Reynolds of West Hartford died August 1, 1966, after a long illness. He was born in Rome, New York, October 6, 1888. He grew up in Schenectady, New York, where he attended Union College in 1911. He was graduated from Albany Medical College in 1940 and then interned for a year at St. Francis Hospital, Hartford. Thereafter he developed a large general practice, which was interrupted by service as a First Lieutenant in the Army Medical Corps in World War I. He was married July 15, 1918 to Nora Walsh and they had two daughters.

In 1924 he left for New York City to specialize in dermatology at the New York Skin and Cancer Hospital, the pioneer skin hospital in the country. After extensive training and experience in dermatology he returned to Hartford and became associated with the late Dr. M. J. Morrissey. For years he was on the attending and later consulting staff at St. Francis Hospital.

Besides being a member of the County and State Societies and the A.M.A. he was a member of the New England Dermatological Society and the Dermatology Section of the New York Academy of Medicine.

He was an ardent and able golfer and an early member of Wampanoag Country Club where he was a member of the House Committee. He was a member of the Church of St. Thomas the Apostle, West Hartford. He is survived by his widow and two daughters, Mrs. Harriett Hatheway of Ellington and Mrs. Virginia Johnston of Worcester, Mass.

He was very social in disposition, but a modest man. By his geniality and desire to help in any worthwhile undertaking, he exerted considerable influence in any organization with which he was connected.

His cordial greeting will be greatly missed, but his memory will long be cherished in the hearts of those who knew him.

WALTER L. HOGAN, M.D.



# Letters To The Editor

## An Ethical Question

### To The Editor:

New ethical issues confront the medical profession as medical science advances, and as medical economics change. Recently questionable practices with regard to clinical research and experiments in humans have come to the fore<sup>1</sup> and other physicians have to answer such questions as: Is it good patient care to insist that a confused elderly couple with cerebral arteriosclerosis fill out its own Medicare forms (Part B) and deal with governmental bureaucracy because the physician holds strong beliefs which dictate that he personally not collect money from the federal government?<sup>2</sup>

The question we wish to raise here is an old one but new for Connecticut (and Massachusetts) physicians, thanks to changes in the laws governing conception control. Can a physician deny in good conscience a patient information, instruction and devices for family planning because of his personal beliefs and values? It is a well-established fact that good maternal and infant health are inversely related to multiparity and family size, besides varying significantly with racial and socioeconomic factors. Furthermore, a woman's emotional health and the psycho-social welfare of her family, another aspect of total health, are contingent on child spacing appropriate to her psychological and emotional resources.<sup>3</sup> It has further been established that effective family planning must be a part of total and integrated health care, and that advice and prescription for family planning is best initiated early in the post-partum period by the physician who delivered the baby.<sup>4</sup> How does a physician justify failure to initiate appropriate recommendations, let alone refusal to arrange for this part of medical care when requested?<sup>5</sup> Is it good or even permissible practice to operate on a patient, and then ignore issues of aftercare, maybe because the surgeon doesn't believe in rehabilitation?

Physicians have traditionally set aside their standards and personal feelings when saving the lives of suicidal patients, of criminals, or of enemy casualties on the battle field. What are the ethics of refusing to initiate family planning measures which safeguard maternal and family health, which prevent family pathology and the birth of emotionally undernourished children whose parents didn't want them in the first place—consciously or unconsciously. How many physically battered children appear in our emergency rooms because some physician put his own values above medical needs and indications?<sup>6</sup> There are now no legal barriers to the implementation of professional judgement and knowledge concerning family planning; only the physician's choice between his personal beliefs and his professional knowledge and competence determines the fate of many a family for better or worse with regard to keeping the number of offspring within the limits of the family's resources for emotional, educational and tangible nourishment.

STEPHEN FLECK, M.D.

Yale University School of Medicine,  
Department of Psychiatry,  
New Haven, Conn.

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### To The Editor:

Please accept the sincere and grateful thanks of the Connecticut Division for your interest and assistance in making the two cancer issues of CONNECTICUT MEDICINE possible.

We have already received several highly complimentary comments concerning the editorials and articles appearing in these two issues and feel this material will be of special value to Connecticut physicians.

There is also a good deal of interest being expressed in the article, "Nursing The Patient With Cancer—An Exercise In Timing", by Virginia Barckley, Cancer Society Nursing Consultant, which appeared in the June issue of your *Journal*. In this connection, The Connecticut Nurses' Association would like very much to reprint Miss Barckley's article in one of the fall issues of their publication, *Nursing News*, and have asked me to seek the permission of your *Journal* to reprint this article. Proper credit would, of course, be given to CONNECTICUT MEDICINE.

Your cooperation in this matter will be greatly appreciated.

Sincerely,

(Miss) JEANE M. ROTH

Education Director

American Cancer Society Connecticut Division, Inc.

New Haven, Conn.

### To The Editor:

CONNECTICUT MEDICINE should be complimented for its August 1966 issue. Continuing medical education is essential to all physicians. Your journal certainly serves as one of the important facets for continuing medical education. I find it so.

Sincerely,

JOSEPH WEINER, M.D.

New Haven, Conn.

*Letters to the Editor are welcome and will be published for informative and educational purposes as space permits. As with other material which is submitted for publication, all letters will be subject to the usual editing. Address all correspondence to: THE EDITOR, CONNECTICUT MEDICINE, 160 St. Ronan Street, New Haven, Connecticut, 06511.*

## Special Notice

### SEMINAR ON PERINATAL MORTALITY

sponsored by

THE CONNECTICUT STATE MEDICAL SOCIETY  
STATE OF CONNECTICUT DEPARTMENT OF HEALTH  
YALE UNIVERSITY MEDICAL SCHOOL

**Wednesday, November 16, 1966—9:00 A.M.—5:30 P.M.**

Mary Harkness Auditorium — 333 Cedar Street, New Haven, Connecticut

Morning Chairman—Samuel D. Rowley, M.D.,  
Department of Pediatrics, Hartford Hospital.

#### INTRODUCTION—PERINATAL PROBLEMS

Robert E. Cooke, M.D., *Chairman*, Department of Pediatrics, Johns Hopkins University School of Medicine.

#### PROBLEMS OF NUTRITION (Screening Methods & Data)

Robert K. L. Nesbitt, Jr., M.D., *Chairman*, Dept. Obs-Gyn, Syracuse University College of Medicine.

Coffee Break

#### SOCIO-ECONOMIC FACTORS INVOLVED IN PERINATAL PROBLEMS

Arthur Lesser, M.D., *Deputy Director*, Children's Bureau, Washington, D.C.

#### EFFECTS OF DRUGS AND OTHER AGENTS—INCLUDING ANESTHETIC AGENTS—ON THE INTRA-URINE PATIENT

Jerold F. Lucey, M.D., *Associate Professor of Pediatrics*, University of Vermont Medical School.

#### PANEL DISCUSSION (Audience Participation)

Moderator—Sydney Gellis, M.D., *Chairman*, Department of Pediatrics, Tufts Medical School.

Lunch

Afternoon Chairman—Charles D. Cook, M.D., *Chairman*, Department of Pediatrics, Yale Medical School.

#### RECENT ADVANCES IN NEONATAL RESEARCH

Louis Gluck, M.D., *Director*, New Born Services Yale Medical School.

#### LABORATORY AND PATHOLOGICAL ASPECTS OF THE PLACENTA, FETUS AND NEWBORN

Kurt Benirschke, M.D., *Chairman*, Department of Pathology, Dartmouth Medical School.

#### NEWER TECHNIQUES AND EQUIPMENT IN PRE-MATURE CARE

William Silverman, M.D., *Professor of Pediatrics*, Babies Hospital, Columbia-Presbyterian Medical Center, New York.

Coffee Break

#### PANEL DISCUSSION—POSTNATAL FACTORS (Audience Participation)

Moderator—Sydney Gellis, M.D.

#### WHAT CAN WE DO?—A SUMMATION

Sydney Gellis, M.D.

## BOOKS RECEIVED

*Books received for review are acknowledged in this department and such acknowledgement must be regarded as a sufficient return for the courtesy of the sender. Selection will be made for review in the interests of our readers and as space permits.*

*Cardiovascular Surgery 1965.* American Heart Association Monograph Number Thirteen. Edited by F. A. Simeone, M.D. Council on Cardiovascular Surgery, American Heart Association, 1966. 203 pp. \$3.00.

*Symposium On Cerebrovascular Disease.* American Heart Association Monograph Number Fourteen. Edited by Robert G. Sickert, M.D. American Heart Association, 1966. 48 pp. \$2.50.

*Hematologic Problems In The Newborn.* Frank A. Oski, M.D. and J. Lawrence Naiman, M.D. Volume IV in the Series Major Problems in Clinical Pediatrics. Alexander J. Schaffer, Consulting Editor. W. B. Saunders Co., Philadelphia and London, 1966. 294 pp. Price not specified.

*Stereoscopic Atlas Of Mastoidotympanoplastic Surgery.* Harold F. Schuknecht, M.D., Werner D. Chasin, M.D. and John M. Kurkjian, M.D. The C. V. Mosby Co., St. Louis, 1966. With 51 figures and 70 stereoscopic views in color on 10 View-Master reels keyed to labeled drawings and figures, and a View-Master compact viewer. 92 pp. \$26.50.

*Atlas Of Hernia Repair,* Carl H. Calman, M.D. The C. V. Mosby Co., St. Louis, 1966. Illustrated. 159 pp. \$16.75.

*Encyclopedia for Medical Assistants.* Louis Brachman, M.D. Cathedral Square Publishing Co., Wisconsin, 1966. 448 pp. Price not specified.

*Early Management of Acute Trauma.* Alan M. Nahum, M.D. The C. V. Mosby Company, St. Louis, Missouri, 1966. 336 pp. with 271 figures. \$21.00.

*Synopsis of Neurology.* Second Edition. Francis M. Forster, B.S., M.D. The C. V. Mosby Co., St. Louis, Missouri, 1966. 218 pp. \$7.50.



# MOLECULAR REMODELING—

*laboratory exercise or clinical necessity?*

More than twenty-five years have passed since the discovery of the diuretic activity of sulfanilamide started pharmacologists on a succession of molecular remodelings to find the ideal diuretic.

## Diuresis—a sought-after clinical effect from an unwanted side effect

It started in 1937 when a clinician reported that the administration of a sulfonamide was sometimes accompanied by an unexplainable side effect—metabolic acidosis.<sup>1</sup> Three years later the side effect was explained. The sulfonamide radical of sulfanilamide inhibited carbonic anhydrase,<sup>2</sup> the enzyme responsible for converting carbon dioxide and water to hydrogen ions and bicarbonate ions.

Later, other investigators showed by dog experiments that metabolic acidosis probably resulted when the inhibition of carbonic anhydrase upset the exchange of hydrogen and sodium ions, causing increased excretion of sodium as the bicarbonate.<sup>3</sup>

It was twelve long years after the first report of the unexplainable side effect (metabolic acidosis) that it was finally shown that large doses of sulfanilamide administered to edematous patients were indeed capable of promoting diuresis.<sup>4</sup> However, the possibility of toxic effects from its prolonged use and its relatively weak diuretic action made it impractical for clinical use as a diuretic.<sup>5</sup>

Because the inhibition of carbonic anhydrase seemed to be the key to effective diuresis, investigators began to look for more potent enzyme inhibitors—in the hopes that they would be more effective diuretics.

The most important of these early compounds, acetazolamide, enjoyed several years of fairly wide clinical use.

Its carbonic anhydrase inhibitory activity was several hundred times greater than that of sulfanilamide.<sup>6</sup> The increase in inhibitory activity, however, increased not only the excretion of sodium and bicarbonate ions, but also the excretion of potassium.<sup>7</sup> And, like its predecessor, acetazolamide precipitated mild acidosis. Its prolonged use could result in hypokalemic acidosis.<sup>7</sup>

## The 'thiazides'—an answer to the metabolic acidosis caused by carbonic anhydrase inhibition

Despite the fact that the sulfonamide

group appeared to be responsible for carbonic anhydrase inhibition which in turn appeared to be responsible for diuresis, investigators began to synthesize compounds with structural alterations to the sulfonamide group.

The first major breakthrough came with the synthesis of chlorothiazide. Altering the sulfonamide group did indeed alter the ability of chlorothiazide to inhibit carbonic anhydrase—it was only 1/10th as potent as acetazolamide in inhibiting the enzyme.<sup>8</sup> Despite the drop in inhibitory potency, however, chlorothiazide proved to be an effective diuretic—an observation that led to the conclusion that its diuretic action was due to some mechanism other than its action on carbonic anhydrase.<sup>9,10</sup>

For effective diuresis, chlorothiazide was administered in daily dosages ranging from 250 to 2000 mg.<sup>11</sup> It increased the excretion of sodium and chloride; and, to a lesser extent, potassium and bicarbonate.<sup>11</sup> The excretion of potassium appeared to be maximal at higher dose levels at which, theoretically, the carbonic anhydrase inhibitory effect is more active.<sup>11</sup> Its prolonged use, therefore, could sometimes result in metabolic hypokalemic, hypochloremic alkalosis.<sup>7</sup>

## Naturetin—effective diuresis with more favorable electrolyte balance

Other thiazides followed—with improvements being aimed at two particular areas: 1. attempts to increase diuretic action in relation to the milligram potency of the drug, and 2. attempts at a more favorable sodium/potassium ratio in the urine, i.e., to decrease the excretion of potassium while maintaining the excretion of sodium.<sup>12</sup>

One of these, Naturetin, Squibb Bendroflumethiazide, has made advances on both these points. "By adding a 3-benzyl radical to hydroflumethiazide a rather dramatic reduction in dose range is accomplished. With this drug, effective sodium excretion is obtained with

doses between 2.5 and 10 mg., which is a 200 to 1 ratio as compared to chlorothiazide..."<sup>13</sup>

Moreover, due probably to its virtual lack of carbonic anhydrase inhibition, Naturetin (bendroflumethiazide) has been shown to cause less potassium and bicarbonate loss and less alteration in urinary pH than either chlorothiazide or hydrochlorothiazide.

Naturetin is outstandingly effective not only in establishing, but also in maintaining, excretion of retained fluid in edematous patients. And its duration of action is sufficiently prolonged to allow a single daily administration in most patients. Naturetin is also an effective antihypertensive agent.

**Contraindications:** Severe renal impairment; previous hypersensitivity.

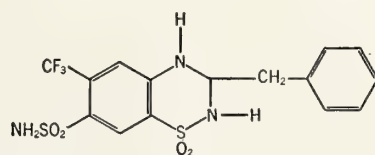
**Warning:** Ulcerative small bowel lesions have occurred with potassium-containing thiazide preparations or with enteric-coated potassium salts supplementally. Stop medication if abdominal pain, distension, nausea, vomiting, or G.I. bleeding occur.

**Precautions:** The dosage of ganglionic blocking agents, veratrum, or hydralazine when used concomitantly must be reduced by at least 50% to avoid orthostatic hypotension. Electrolyte disturbances are possible in cirrhotic or digitalized patients.

**Side Effects:** Bendroflumethiazide may cause increases in serum uric acid, unmask diabetes, increase glycemia and glycosuria in diabetic patients and may cause hypochloremic alkalosis, hypokalemia; cramps, pruritus, paresthesias, and rashes may occur.

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## NEW BOOKS IN REVIEW

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### **THE THEORY AND PRACTICE OF PSYCHIATRY.**

**Frederick C. Redlich, M.D. and Daniel X. Freedman, M.D. Basic Books Publishers, New York, 1966. 880 pp. \$12.50.**

Reviewed by: LOUIS H. NAHUM

Heretofore psychiatry's chief methods have been to listen, to observe, rather than to manipulate and to act. Its chief interests have been biographic and its procedures are those of history. It is therefore not surprising and indeed most welcome that the first eleven chapters of this book are devoted to development of psychiatric thought with particular emphasis on the differentiation of fact from dogma. One might say that psychiatry shows the ambivalence of Greek civilization which at one and the same time gave birth to the scientific method in medicine while being shot through with exotic religious beliefs with bizarre rites and rituals to appease angry spirits. Psychiatry still shows the marks of both trends.

Freud's monumental contribution was directed to the scientific study of the dynamics of human personality. By means of psychoanalysis he exposed the power of the unconscious, of the life and death instincts and their operation in the ontogenesis of human behavior. His contributions have had far ranging influences upon anthropology, sociology, literature and art. They have become of paramount importance not only for psychiatry but in the management of all sick and even all well people. We may say that one of the principle contributions of psychoanalysis to medicine lies in its humanizing influence. It has kept Man at the center of its concern rather than his enzymes or the chains of proteins of which he is composed. Nevertheless Freud warned psychiatrists that they would have to hurry up with their investigations because the people with the test-tubes were at their heels.

His predictions are all too true today. There has developed a ferment in mental science, and a ground swell in the physiologic chemical and neurologic aspects which caused leaders of psychiatric thought to hope that sooner or later fundamental knowledge will lead to a unified concept giving a physiologic basis to mental illness. This trend can be seen in such provocative studies of J. P. Scot on the critical periods of behavioral development, of Levin and his group on the role of hormones on the organization of the nervous system and that of Kleitman and also Fischer on the neurophysiology of dreaming sleep. This trend is being followed in the development of new institutions devoted to behavioral science at Stamford, at the Rockefeller University and was long ago perceived at Yale in the founding of the Institute of Human Relations in which the two authors of this book have functioned and established a celebrated Department of Psychiatry.

The recognition that psychiatry is presently an applied medical science and will increasingly rest on the foundations of biological and behavioral sciences is the basic philosophy of this excellent text. Psychology, sociology, anthropology, and the biologically oriented behavioral science of psychanalysis are fused in one grand design. Its humanistic dimension

is evident in its emphasis on social welfare, education and the law. However, it is an eclectic approach which the authors have rightly chosen because in the present state of our knowledge no unifying principles have as yet been uncovered which would adequately explain the field. No area of psychiatry has been neglected, no attitude is allowed to dominate.

What we need to know is how behavior becomes structured from infancy to adulthood, what the socializing forces are, how behavior becomes disorganized, where is dogma used as a mask for our ignorance and our doubts, what are the unsolved problems. This is a tall order for even the most learned and competent in the field. It requires profound learning, critical judgment, historical background and absence of dogmatism. The reader will find these qualities admirably displayed in this excellent volume, which is the outgrowth of the experiences, thinking and practice of psychiatry at Yale.

The chapter on neuropharmacology is excellent. The section on child psychiatry by Lustman is an especially creditable job considering the limitation of space allotted to it. Normal psychodynamic ontogenesis is greatly abbreviated for this reason, although the Child Development Center at Yale is rich in material on this aspect of psychiatry.

The section on psychoanalysis is quite short, largely because of its limitations in psychotherapy and perhaps because the authors implied hope for the appearance of a physiologic explanation for neurotic behavior.

The section on schizophrenia is especially expanded and reflects the intense interest in the authors' department in this protean manifestation of behavioral disorganization. Being influenced largely by communication theory, they see this devastating disorder as a form of failure of communication although they do not neglect to deal with the possible organic causes, none of which have stood up under continued investigation.

It is obviously impossible in one volume to do other than to simplify and condense the vast mass of accumulating knowledge and diverse directions the field of psychiatric practices have taken, other than to present an authoritative objective survey of modern psychiatry. This the authors have achieved with great distinction. The book is beautifully written with flow of language and precise semantics making it a literary product of high quality.

This book is excellent for second year students, for the many different types of psychiatrists and for the physician who will come more and more to be an active participant in treating behavioral problems in connection with general sickness. It will be of inestimable help to other professionals working in the area of mental health such as social workers, community administrators, legislators and especially lawyers and judges.

All in all Professors Redlich and Freedman have in this book done psychiatry and medicine a great service.

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**HIDDEN HIERARCHIES: The Professions and Government** by Corrine Lathrop Gilb, Ph.D. Harper and Row, 1966. 247 pp. \$5.95.

Reviewed by: J. ALFRED FABRO

"Hidden Hierarchies" is well worth reading. Any physician who is interested in the role and relationship of his profession to government and to the law-making process should enjoy and learn from it.

Dr. Gilb, a sociologist, directs our attention to the interaction and political relationships between our state and national governments on the one hand and the many professional organizations in the U.S.A. on the other. The increasing power of government is self-evident, but the balancing effect of power through organized groups, such as professional associations, unions, veterans' groups, farm and church societies, chambers of commerce, and the like is not so evident.

She uses the voluntary professional associations, medical and legal especially, to show that, as much as the individual may dislike the disadvantages of organization, he stands to retain his freedom better therein than alone, because organizations provide a balance of power to the increasing role of government in our lives.

Why does she use the professions as a point of departure in her approach to the problem? Because along with the political tendency toward centralization, nationalization, and bureaucratization of government, she sees the development of an "age of professionalism," with a multiple of professions developing political power through organization to occupy a half-way, quasi-public zone between public and private spheres in our political system.

She takes the reader through the historical development of the professions in Western society. First was the medieval guild with its characteristics of long apprenticeship, self-government, regulation of standards of craftsmanship, and regulation of fees. Then the "Adam Smith era": the individualistic, competitive, non-regulated, free enterprise period beginning in America the end of the eighteenth century. And in the nineteenth century, the development of national professional organizations modeled on our national political system with constitutions and representative government. These national professional organizations, however, were also interested in developing a confederation of strong, competent, state organizations, especially since most public laws affecting and regulating the professions were (and are) passed at state level. (The AMA was founded in 1847 and federated in 1901). The nineteenth century was a period when the professions sought to improve and regulate standards by advocating licensing, by state agencies controlled by the profession.

And now, as she states, we are entering an "age of professionalism." More and more occupations are striving for recognition of professional status. They realize that they can accomplish their aims and improve their status through organization. By this means, they put concentrated pressure on legislatures for legislative recognition and licensing.

One of her most interesting and informative chapters is devoted to the relationships between state legislatures and the organized professions. She deals with the role and importance of the lobbyist, acting in a legitimate advisory role to the

legislature. It is this area in which the better organized professions will contribute the most, and best protect the interests of their members. She stresses that legislatures in the Anglo-American tradition are for the most part passive, reactive, receptive, pragmatic, and piece-meal in their approach to legislation. They need and use the expert. The professional through organization can play an important role in the legislative process. Alone, he is ineffective.

She posits the paradox that is not a paradox: "... freedom in a complex, interdependent economy comes through organizations. Without an organization to define and sustain his areas of freedom, the average individual in a profession would often not be able to be free. The paradox is not a real paradox at all."

I agree with her premise and believe her book is timely. Especially now more than ever before we physicians—in private practice, in research, in teaching, in public health—all of us need to reassess the role of our associations in relation to ourselves, our profession, to society, and to the government. The Surgeon General has stated the obvious: he must supervise the manner in which public money is spent. The President has appointed a committee to decide whether there is a proper balance between "pure" research and applied medicine. How much did the universities and medical schools as an organized and coherent body participate in the report on "A National Program to Conquer Heart Disease, Cancer, and Stroke?"

A last point: Dr. Gilb is one of the few writers who has pointed out, without polemics, that the political structure of "organized medicine" is not unique; that it incorporates the American concept of representative government; that it resembles our own federal national government and other voluntary associates. The more important the organization is, the more necessary it is that its leaders reflect the opinions of the members. Does the political structure of the A.M.A. facilitate this?

If you will read Dr. Gilb's book, you will realize that the centralization of our national government will force even more centralization on the professions and analogous groups. In organization, they may be able to keep some of their freedom and to offer a constructive and necessary balance to the State. Centralization means bureaucracy; it can't be avoided. Organization is the price we must pay for freedom.

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## MEDICAL NEWS

### Physicians Warn Of Motorcycle Hazards

The motorcycle is creating a new epidemic in the United States, warn three physicians in the current *Journal of the American Medical Association*.

Alarmed by the number and severity of motorcycle accidents in their own community, the three doctors from Portland, Maine, call for a campaign to reduce motorcycle deaths and injuries.

"It seems clear that the increasing popularity of small motorcycles is creating a serious health hazard in our communities," they said.

Part of the fault is driver carelessness, part is lack of safety devices, and part is due to the public's lack of awareness of special features of motorcycle handling, the physicians said.

"In motorcycle accidents, the victims have no protection whatever. Few helmets are used by the cyclists, and those in use are generally inadequate."

Head injuries are usually much more severe than those in auto accidents, and contaminated, compound fractures are more common, they noted.

"Victims are thrust, often at high speed, into another vehicle or to the pavement. The head receives the full force of impact when the cycle collides with another object, and the cyclist is catapulted over the handlebars."

The authors—two surgeons and a neurologist—saw the effects of such crashes on the patients they treated. From May through August last year, there were 38 victims of motorcycle accidents treated at Portland's Maine Medical Center.

Three of these victims died. One is blind and paralyzed. Ten suffered fractures of the lower extremities. There were two spinal fractures, two pelvic fractures, two severe abdominal injuries, and nine cases of minor injury to the head and neck.

It was difficult to classify the damage in these accidents, the authors said, because so many victims suffered multiple injuries.

"A most distressing fact is that the group involved are young, otherwise healthy persons. This is not an epidemic involving the aged or the infirm—rather it involves a group of young, healthy people who must be regarded as a most important group in our society."

According to the U.S. Bureau of Vital Statistics, there were 882 motorcycle-accident deaths in 1963. It seems reasonable, the authors said, that there were "far more than a thousand" deaths in 1965.

States need to develop carefully supervised motorcycle driver-training programs, meaningful road tests, and rigid inspection and licensing rules, the physicians said.

"Educational programs in public schools, as well as press and other news media campaigns are needed. Physicians should make themselves available to participate in such efforts in their communities.

"Ways to improve safety equipment, should be sought. Universal use of crash helmets alone would undoubtedly reduce the severity of many injuries."

Multiple injuries are so common in motorcycle accidents that physicians should work in teams in caring for them, the authors said. Skilled, early treatment of severe central-nervous-system injuries and complicated extremity fractures can improve recovery chances, they said.

Finally, the physician noted another aspect of motorcycle crashes: "In many of our cases, parents were opposed to their children having such vehicles. After considerable pressure, the parents reluctantly agreed. When an accident occurred following such a situation, the psychological problems were tremendous."

Physicians should warn parents of the hazards in driving motorcycles, the authors said.

"Only by taking a firm position in combating this rising hazard to health can we expect to avert a great epidemic."

The authors are Richard C. Dillihunt, M.D., George L. Maltby, M.D., and Emerson H. Drake, M.D., all of the Maine Medical Center, Portland.

### AMA Journal Reports On Auto Accidents

A middle-aged man is less likely to have a fatal auto accident in a state which inspects his car regularly, suggests an article in the current *Journal of the American Medical Association*.

If the man is white, he is less likely to die in a car crash than a nonwhite man of the same age, the article says. The reasons for this are complex, but one of the main ones may be that nonwhites generally have lower incomes, and thus drive older, more dangerous cars.

Nonwhite male drivers are more than twice as likely to have a fatal crash if they live in a state which does not inspect vehicles, compared to non-

white residents of states which require twice-yearly inspections, the article said.

The authors, two Harvard Medical School investigators, compared auto-accident death rates in all states, and found that fatality rates were generally higher in states which did not inspect cars for mechanical defects.

The article emphasizes that no reliable method exists for determining the number of fatalities due to auto mechanical failures. The authors said their findings suggest, however, "an association between the preventive procedure of inspection and a lessening of the death rate."

Auto fatality rates vary widely from state to state. Such factors as geographic area, income, population density, the number of vehicles and the miles they are driven all affect accident rates. But no matter how states were grouped according to these factors, states which did not inspect vehicles had consistently higher auto fatality rates, the authors said.

The authors grouped states according to (1) those which had inspected vehicles for several years, (2) those which began regular inspection since 1960, and (3) those which had no vehicle inspection as of 1960, the date of the last nationwide census.

Between 1950 and 1960, death rates fell about 10 per cent in states which began auto inspection in that period. Death rates increased about 10 per cent during the 10-year period in states which had no vehicle inspections.

"It is widely accepted that automobile inspection is desirable, but in 1960 the states which required inspection were in the minority, and their population was less than 40 per cent of the national total," the authors said.

They also found that between ages 25 and 65, the number of nonwhite men killed in auto accidents exceeds that of white men. The difference is greatest in the 45-to-54 age group.

Why should this be? The article suggests that the age of the cars the men drive has something to do with it.

A tabulation by the U.S. Bureau of the Census indicates that only 32 per cent of 45-to-54-year-old men who are heads of households own cars more than six years old. But among nonwhite men in this group, 46 per cent own cars that are six years old or older.

Older cars are more likely to be involved in accidents; the fatal-accident rate of cars over eight years old is more than twice that of cars less than two years old.

"A number of organizations, including the American Automobile Association, believe that a

statewide system of state-owned or state-designated inspection stations should be maintained in every state or that, as an alternative, on-the-road inspections should be carried out on a continuing basis," the article said.

The hazards associated with older cars and the influence of vehicle inspection merit considerable investigation, the authors said. They are Robert C. Buxbaum, M.D. and Theodore Colton, Sc.D., both of the Department of Preventive Medicine, Harvard Medical School, Boston, Mass.

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 in any case,  
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## Therapy:

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 (initial adult dose)

**indications:** Urinary tract infections caused by gram-negative and some gram-positive organisms.

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**references:** (1) Based on 23 clinical papers, 1512 cases. Bibliography on request. (2) Bush, I. M., Orkin, L. A., and Winter, J. W., in Sylvester, J. C.: *Antimicrobial Agents and Chemotherapy*—1964, Ann Arbor, American Society for Microbiology, 1965, p. 722.

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# Connecticut Medicine

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# Connecticut Medicine

Connecticut State  
Medical Journal

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## SCHEMA OF ATHEROPHILIA

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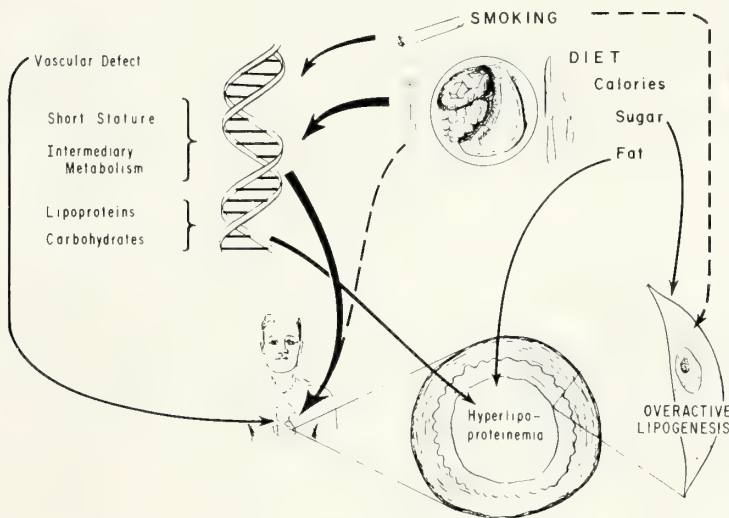


Figure II of *Circulation*, Volume XXXIII, May, 1966, entitled, "A Study of Coronary Heart Disease in Young Men." By Doctors: Frederick T. Hatch, M.D., Ph.D., Pentti K. Reissell, M.D., Theo. M. W. Poon-King, M.D., George P. Canellos, M.D., Robert S. Lees, M.D., and Lillian M. Hagopian, B.S.



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# Connecticut Medicine

## editorials

### Science Tools: 22. Diagnosis By Ultrasound Echo

Most investigators using ultrasound for diagnostic purposes use the technique for recording reflected ultrasound. This technique utilizes the principle that when ultrasound crosses a boundary or interface between two media with different acoustical impedance, some of the waves are reflected while others continue through the second medium. Thus ultrasound will be reflected by an interface between gas and liquid, liquid and solid, or solids of different densities. The amount of sound that is reflected depends upon the magnitude of the acoustical difference between the two media, and like light, the angle of incidence of the ultrasonic beam with the interface.

The technique requires a transducer which is capable of emitting and also receiving ultrasound. The transducer transmits 1  $\mu$  sec ultrasound impulses intermittently at rates of either 200, 1,000 or 2,000 times per second. In between the impulses, the transducer acts as a receiver and records the reflected sound waves (echoes) which now activate a crystal of quartz or barium titanate and are converted into electric signals which can be displayed on an oscilloscope. Since the velocity of sound in human tissues is known (1540 m (sec))<sup>1</sup> the time interval between transmission of the sound and return of the echo can be used to measure the distance between the interface and the transducer. Commercial ultrasonoscopes actually perform the calculation electronically and the distance between transducer and echo is displayed directly on the oscilloscope.

When the transducer is stationary one records only those interfaces which are perpendicular to the transducer at any particular angle and location. Such recordings are one-dimensional. Attempts are also being made to achieve compound scanning

through two-dimensional recordings. With this technique the transducer is moved and multiple one-dimensional tracings are obtained from different positions and are combined to give a two-dimensional recording resembling a cross-sectional view of the object being examined. The technique gives far more anatomical information and is theoretically superior to the simpler method. However, it requires much more elaborate equipment and has some definite problems not yet solved.

The primary advantage of ultrasound echo over diagnostic x-ray is that its capability for distinguishing interfaces between objects of different densities is far more sensitive than x-ray. There are a large number of substances that are not radio-opaque but which can be detected easily with the ultrasound. For example, it is very simple for ultrasound to distinguish between liquid and human soft tissue, a differentiation virtually impossible with x-ray. A practical application of this type is the use of ultrasound in detecting pericardial effusions.<sup>2</sup> It will undoubtedly replace the x-ray in this instance.

Another advantage of ultrasound is that in the power levels used for diagnostic purposes it has been shown thus far to be completely harmless. Ultrasound examinations have been done on literally thousands of patients all over the world in the last ten years without a single untoward reaction. These harmless clinical results have been confirmed experimentally on animals. As a result ultrasound is being used as a substitute for x-ray merely to avoid the hazard of radiation. An example of this is its use in obstetrics.<sup>1</sup>

Yet another valuable feature of ultrasound is that many of the medical applications can be done with commercially available equipment which is portable thus permitting the examination to be done at the bedside. Thus the technique is ideal

## THE COVER

### SCHEMA OF ATHEROPHILIA

SCHEMATIC representation of the complexity of the environmental and hereditary influences which may accelerate the progress of human atherosclerosis. The present study leads to the conclusion that the incriminated environmental factors play their role largely through interaction with genetically determined capacities of pathways of intermediary metabolism and properties of arterial tissue. This may account for the great variability in the patterns of abnormal findings among the young men with coronary heart diseases.

for the many patients who may be critically ill and should not be moved.

The most popular use of ultrasound is the detection of the midline of the brain. This examination provides a simple method of determining whether or not there has been a shift of the midline due to a space occupying lesion. As a screening test for patients with head injuries, this technique has been particularly helpful. The examination takes from 5-20 minutes and the accuracy and reliability of the results have been confirmed by dozens of investigators.<sup>1</sup>

Probably the next most common application of diagnostic ultrasound is in the field of cardiology.<sup>3,4</sup> It is possible to record consistently an echo from the anterior leaflet of the mitral valve. The pattern of movement of the echo is fairly characteristic for patients with or without mitral stenosis. The differences are so distinct that the degree of stenosis can be quantitated with reasonable accuracy. So much so that many centers have already substituted ultrasound for cardiac catheterization when evaluating patients for mitral commissurotomy. The ultrasound echo has been used to detect left atrial tumors, tricuspid valve motion and a host of other intracardiac structures. One echo apparently originates from a portion of the left ventricle near the mitral annulus and this may prove to be both of investigative and clinical value.

There have been literally dozens of other medical uses for diagnostic ultrasound. Ophthalmologists have used it to remove foreign bodies from the eye.<sup>5,6</sup> Obstetricians have been measuring the biparietal diameter of the fetal head in utero. Surgeons have used ultrasound echo to probe for gall stones in the common duct at the time of surgery.<sup>7</sup> Compound scanning has been used to examine practically every organ of the body; the head, the eye, pelvic organs, breast, liver, kidneys, and spleen have thus far received the most attention.

There are of course limitations to the method. The sound wave does not travel well in gas. For example, it is more difficult to examine the heart in pulmonary emphysema. There is also some subjective element in the procedure because in most instances the transducer is held by hand and a slight change in angulation of the transducer may yield misleading results. Changes in the electronic controls will also alter the recordings. Thus it may be difficult to compare the results of similar examinations by two different people or by two different ultrasonoscopes.

The problem of standardization of the equipment and the recording techniques is a difficult one. There is the variability of one patient from another which prohibits any rigid type of standardization. This is especially a problem for in-

vestigators who are using the more complicated compound scanning techniques. Actually it is not nearly as critical in the relatively simple one-dimensional use of ultrasound.

Despite these obvious difficulties and limitations many of the practical applications have already become accepted as routine diagnostic procedures. It may be expected that more investigators will turn to this technique and that undoubtedly many additional medical uses will be developed and that it will probably play an increasingly important role as a medical diagnostic procedure.

L.H.N.

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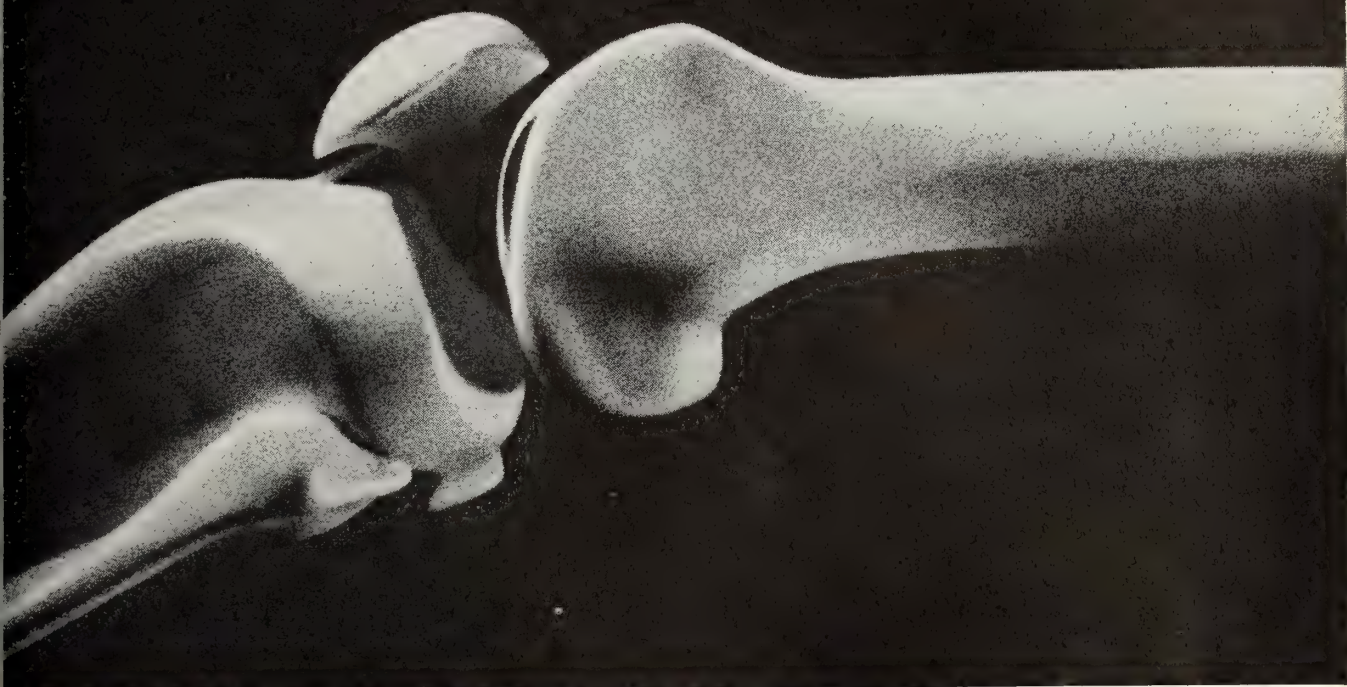
## The Microcirculation (M.C.): II. Clinical Syndromes

Four etiologic factors can each produce the same end result—failure of M.C. perfusion, cardiogenic shock, traumatic, hemorrhagic and endotoxic shock. Once the perfusion rate of the terminal vascular bed becomes inadequate, there develops vasoconstriction, metabolic acidosis, and changes in the clotting mechanism. Each of these factors, interact aggravate and perpetuate each other.

The important point to be made here is that our attempts to correct the initial factor as for example by digitalization, blood replacement, fluid replacement or antibiotic therapy in the case of endotoxic shock will not succeed alone, until the vasoconstriction, acidosis, or microthrombosis are also intensely treated. This will involve the use of sympatholytic drugs, sodium bicarbonate to combat acidosis and desludging agents notably dextran 40 to overcome the microthrombosis. Such measures to combat shock would probably best be carried out by "shock teams" which could operate with remarkably simple portable equipment.

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Edema; danger of cardiac decompensation; history or symptoms of peptic ulcer; renal, hepatic or cardiac damage; history of drug allergy; history of blood dyscrasia. Because of the increased possibility of toxic reactions, the drug should be used with greater care in the elderly and should not be given when the patient is senile or when other potent chemotherapeutic agents are given concurrently. Large doses of Butazolidin alka are contraindicated in patients with glaucoma.

### Warning

If coumarin-type anticoagulants are given simultaneously, the physician should watch for excessive increase in prothrombin time.

Pyrazole compounds may potentiate the pharmacologic action of sulfonylurea, sulfonamide-type agents and insulin. Patients receiving such concomitant therapy should be carefully observed for this effect.

Use with caution in the first trimester of pregnancy.

### Precautions

Before prescribing, the physician should obtain a detailed history and perform a complete physical and laboratory examination, including a blood count. The patient should be kept under close supervision and should be warned to report immediately fever, sore throat, or mouth lesions (symptoms of blood dyscrasia); sudden weight gain (water retention); skin reactions; black or tarry stools. Regular blood counts should be made to guard against blood dyscrasias.

### Adverse Reactions

The most common adverse reactions are nausea, edema and drug rash. Moderately lowered red cell count may sometimes occur due to hemodilution. The drug has been associated with peptic ulcer and may reactivate a latent peptic ulcer. Infrequently, agranulocytosis, exfoliative dermatitis, Stevens-Johnson syndrome or a generalized allergic reaction may occur and require withdrawal of medication. Stomatitis, salivary gland enlargement, vertigo or languor may occur. Leukemia and leukemoid reactions have been reported but cannot definitely be

attributed to the drug. Thrombocytopenic purpura and aplastic anemia are also possible side effects.

Confusional states, hyperglycemia, agitation, headache, blurred vision, optic neuritis and transient hearing loss have been reported, as have hepatitis, jaundice and several cases of anuria and hematuria. With long-term use, reversible thyroid hyperplasia may occur infrequently.

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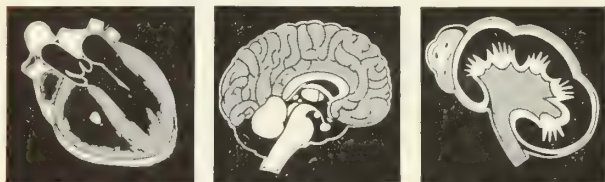
# Geigy



# Behind continued high blood pressure readings lies the possibility of organic damage<sup>1-13</sup>

**M**ANY OF THE aspects of essential hypertension are unpredictable—either because there are a number of mechanisms involved or because individuals differ in their responses to these mechanisms.<sup>1</sup>

There is one aspect of hypertension, however, that seems, in many cases, predictable. "... when the blood pressure is elevated to a marked degree for an adequate period of time, this in itself leads to perpetuation of the syndrome with resulting vascular damage throughout the body."<sup>14</sup> All too often the disease progresses until there is damage to one of three vital organs: the heart, the kidney, the brain.



"Hypertension is certainly a major factor in the genesis of coronary heart disease, and it is even more important when compounded with obesity."<sup>4</sup>

"[Vascular deterioration] can be clearly seen in the kidney with a degree of damage that can be measured by renal function studies."<sup>10</sup>

"... most evidence suggests that reduction of blood pressure, when it is too high, not only relieves the heart of excess work but reduces vascular damage."<sup>1</sup>

**"In short, treatment is indicated."<sup>1</sup>**

Antihypertensive therapy will not restore the blood vessels to normal. Yet many of the vascular changes and symptoms caused by increased blood pressure may be arrested or alleviated when the blood pressure is reduced to normotensive levels.<sup>7</sup>

Reducing the blood pressure helps curtail further vascular damage and improves the prognosis — when damage is not too far advanced before therapy is started.<sup>14</sup> Essential hypertension is an indication not only for treatment, but for early and adequate treatment of the patient in question.

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**References:** 1. Page, I. H., and Dustan, H. P.: The Usefulness of Drugs in the Treatment of Hypertension, in Ingelfinger, F. J.; Relman, A. S., and Finland, M.: Controversy in Internal Medicine, Philadelphia, W. B. Saunders Co., 1966, p. 95. 2. Hollander, W.: The Evaluation of Antihypertensive Therapy of Essential Hypertension in Ingelfinger, F. J.; Relman, A. S., and Finland, M.: Controversy in Internal Medicine, Philadelphia, W. B. Saunders Co., 1966, p. 97. 3. Nickerson, M.: Antihypertensive Agents and the Drug Therapy of Hypertension, in Goodman, L. S., and Gilman, A.: The Pharmacological Basis of Therapeutics, ed. 3, New York, The Macmillan Co., 1965, p. 727. 4. Berkson, D. M.: Indust. Med. & Surg. 32:371, 1963. 5. Cohen, B. M.: M. Times 91:645, 1963. 6. Lee, R. E., et al.: Am. J. Cardiol. 11:738, 1963. 7. Moyer, J. H.: Am. J. Cardiol. 9:821, 1962. 8. Moser, M.: New York J. Med. 62:1177, 1962. 9. Wood, J. E., and Battey, L. L.: Am. J. Cardiol. 9:675, 1962. 10. Moyer, J. H., and Heider, C.: Am. J. Cardiol. 9:920, 1962. 11. Moser, M., and Macaulay, A. I.: New York State J. Med. 60:2679, 1960. 12. Judson, W. E.: Nebraska M. J. 44:305, 1959. 13. Hodge, J. V.; McQueen, E. G., and Smirk, H.: Brit. M. J. 1:5218, 1961. 14. Moyer, J. H., and Brest, A. N.: Hypertension Recent Advances, Philadelphia, Lea & Febiger, 1961, p. 633. 15. Berry, R. L., and Bray, H. P.: J. Am. Geriatrics Soc. 10:516, 1962. 16. Reid, W. J.: J. Am. Geriatrics Soc. 13:365, 1965. 17. Feldman, L. H.: North Carolina M. J. 23:248, 1962.

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**Dosage and Supply:** Initial dosage, 1 to 4 tablets daily, preferably at meal-time. Maintenance, 1 or 2 tablets daily. Rautrax-N is supplied as capsule-shaped tablets containing 50 mg. Rauwolfia serpentina whole root (Raudixin®), 4 mg. bendroflumethiazide (Naturetin®), 400 mg. potassium chloride.

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quate perfusion pressure successfully combats red blood cell and platelet aggregation but a complicating factor is mechanical trauma to corpuscular elements as well as possible effects of hypothermia. It is the coagulation defect which needs close scrutiny, since even after neutralization by heparin, diffuse oozing or massive hemorrhage may develop. This could be due to two opposite mechanisms. If it is due to an acute fibrinolysis, then anti-fibrinolysin would be indicated. On the other hand, if it is due to intravascular thrombosis and consumption of available fibrinogen then heparin alone could solve the underlying pathology.

Local microcirculatory failure occurs in certain industrial occupations in which repetitive percussion or vibration is present as in air-hammer workers. They develop numbness, tingling, and cold sensitivity. This type of M.C. damage responds neither to heat or cold, possibly because the a-v shunts lose their responsiveness.

The non-freezing cold injury causes first generalized vasoconstriction which is then followed by venular dilation, local leakage from the venules, stasis, capillary necrosis and obliteration. In the meantime the a-v shunts may undergo fibrinoid degeneration. It is a vicious circle which must be broken up at the earliest possible moment. de Takats highly recommends rapid warming (104°F for 30 minutes) and early sympathectomy.

If cold allergy develops the patient exhibits a histamine type of M.C. response, chilblains show fat necrosis, giant cells and perivascular inflammation. Cold agglutinins, cryoglobulins and cryofibrinogens produce cellular aggregates or protein precipitates all of which block the terminal vascular bed, but can be reversed. Most of these responses to cold manifest themselves by Raynaud's phenomenon.

Direct heat from burns produces damage to all segments of the M.C. If the burns are of mild degree, dextran 40 can reduce hemoconcentration, increase blood volume and probably increase the O<sub>2</sub> uptake of the burned tissue. If the burn is of second degree, rapid revascularization and lack of devitalization occurs. If, however, the burns are of third degree, then the entire area becomes avascular and can be delineated by injection of sky or Evans blue which will not stain the necrotic area and thus direct accurate excision.

Electrical injury results in massive intravascular thrombosis, followed by hemorrhage and necrosis. Fibrinolysin may be liberated as a consequence of pain anxiety or cardiac standstill, and this contributes an additional hazard and should be treated vigorously.

Aside from the acute angiopathies there are the chronic ones that need to be borne in mind. In hypersensitivity angiopathies, the endothelium

of the microvasculature acts as a shock organ, develops inflammatory or necrotizing reactions of various intensities to a variety of allergens. Rheumatic arteritis and thromboangitis, obliterates temporal arteries. Delayed vascular reactions after scarlet fever or meningococcus belong in this group, and so may the collagen diseases. Hypersensitivity reactions in skin grafting seem similar to the cell reactions seen in Lupus or in the hadralazine syndrome. Last but not least is the perivascularitis described in patients with renal transplants. In these hypersensitivity reactions of endothelium, immunosuppressive drugs such as steroids seem to help. Nevertheless too fast healing of such a microcirculatory response may lead to necrosis.<sup>1</sup>

In diabetic microangiopathy the small blood vessels reveal thickened basement membranes which later reduplicate and show breaks in continuity as demonstrated with electron microscopic examination of a punch biopsy. The combination of major atheromatous arterial disease, microangiopathy, capillary fragility, and necropathy produces difficult problems in the management of diabetic vascular disease. There is also a growing belief that if one searches for them, early vascular changes can be detected in prediabetic individuals.

In hypertensive arteriolar disease hypertrophy takes place in the muscular wall. A constriction of the lumen and an alteration of the lumen to wall ratio takes place in the minute vessels regardless of the origin of the hypertension. Typical ulcerations occur in the lateral and posterior surfaces of the lower leg with a marked subendothelial hyalinization. When such a lesion is combined with a diabetic or post-phlebitic arteriolar lesion, then its control can only be achieved by wide excision, delayed skin graft and sympathectomy. In such cases with diffuse microvascular lesions, it takes but little trauma to produce it in a given area.

In gout early observers of an attack described a local disturbance of the circulation affecting the venules and capillaries which preceded the redness and swelling. The microvascular disturbance is found to be a reaction to the precipitation of urate crystals and occasionally one can see clefts under the intima under the arteriolar wall. Heparin, de Takats points out, has a remarkable effect on the gouty attack.

During or after vascular reconstruction and even spontaneously atheromatous or cholesterol emboli may break loose. They may be asymptomatic but also may simulate major arterial accidents producing hemiplegia, or renal insufficiency, mesenteric arterial occlusion or peripheral arterial embolism. Often the embolized fragments set up reactions resembling periarteritis nodosa, or foreign body giant cells or even cutaneous nodules. Fur-

thermore if the emboli remain unlysed thrombi may follow.

It is always important to bear in mind the dynamics involved in the transition from cell aggregation to microthrombosis to thrombolysis. Basically all microthrombosis can lead to anemia, hemolysis and depletion of clotting factors. If one encounters increased fibrinolysis at the same time as there is a normal clotting time, then one should suspect the existence of the defibrination syndrome.<sup>2</sup> In this disorder intensive use of heparin will produce a spectacular effect on arresting a hemorrhage which is in fact secondarily due to thrombosis.

Even in the absence of disseminated vascular thrombosis, the red cells may become altered and deformed after the implantation of plastic valves and in the presence of widespread microvascular disease. This is an interesting type of hemolytic anemia resembling that encountered in thrombotic thrombocytopenic purpura.

L.H.N.

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## Transplantation Biology: II. Immunologic Tolerance

*"The time will come when we shall beg portions of skin from a Parent or Friend who is willing to give of his abundance for the relief of a suffering child or neighbor." —George Lawson, 1870.*

When George Lawson wrote these words little did the surgeons of the last century appreciate the formidable nature of the homograft problem. Upward of half a century of research has taught us that homograft destruction is an immunological phenomenon, the outcome of a highly specific attack on the part of the host against foreign genetically determined cellular isoantigens known now as transplantation antigens.

By the early 1950's various means of prolonging the life of homografts in experimental animals had been discovered, including x-irradiation and administration of steroid hormones to the host. Most important of these was the discovery that if very young animals were inoculated with suspensions of living homologous cells, they may be rendered completely and specifically incapable of reacting against subsequent grafts from the donor of the permanently inoculated cells in later life without impairment of their well being. This induced specific state of unresponsiveness of antigenic material is known as immunological tolerance.

Once it was established that the immunological

problem was soluble at least in principle, geneticists, immunologists, surgeons, biochemists and others in ever increasing numbers began to focus their attention upon the chemical homotransplantation of organs. Whether one is concerned with transplantation of living tissues for experimental or therapeutic purposes, problems of two quite distinct categories are involved.

The first of these includes problems concerned with the act of transplantation itself. These are said to be of an essentially technological nature. Of course there must be procurement, preparation, temporary storage and finally the relocation of the graft in a living organism. It must be done in such a manner that the normal healing processes can occur in conjunction with vessel and duct anastomoses where necessary. By this means it is hoped to procure the viability and conservation of normal structure and function. Regardless of how well the technological aspect is properly carried out, the lymphatic system of an organ is not restored and the effect of this loss of lymphatic drainage upon continued health of the transplanted cells is a big question mark in their ultimate viability.

The technical possibility of replacement by grafting of bone marrow, lymphoid tissue and corneas, does not involve lymphatic deprivation. However, when it comes to extensive areas of skin some endocrine organs such as ovaries, parathyroids may not suffer too much from deprivation of lymphatic drainage, though their indefinite viability may. However, kidneys, hearts, lungs, liver, uterus, segments of small intestines, and entire limbs certainly must suffer from lymphatic drainage deprivation. Nevertheless on the basis of extensive work on dogs and other animals, in most cases substantiated by trials on man, the technical feasibility of replacement by grafting has been established.

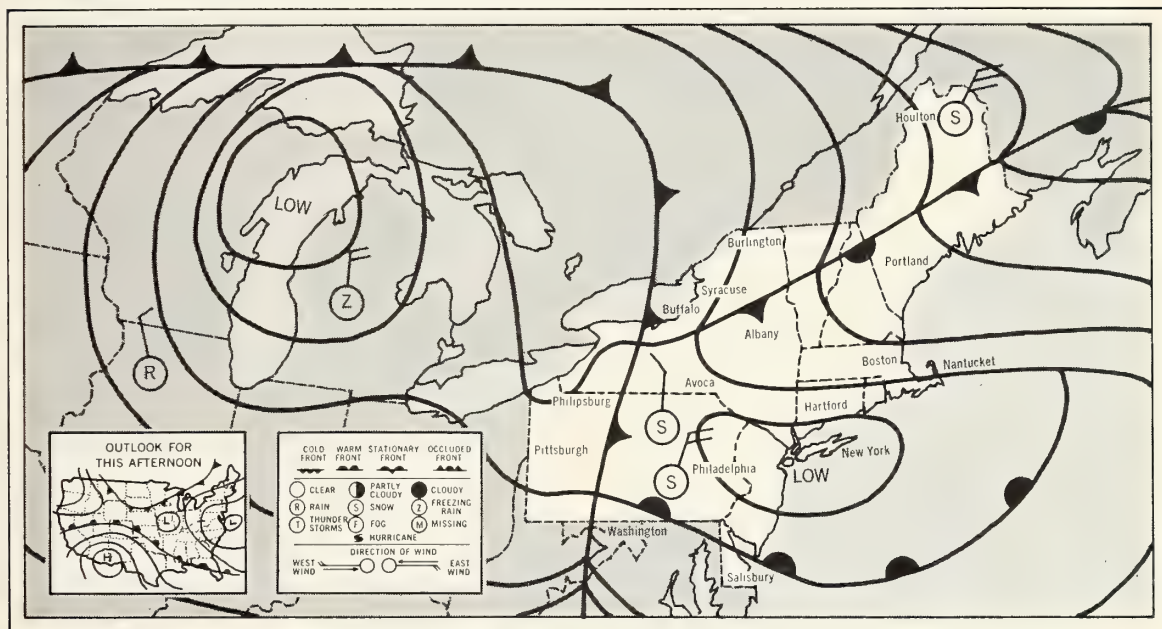
There is still great scope for future investigation and improvement. For example, it is well known that a sheet of skin, provided it is not too thick, when grafted to a clean vascular bed and held in place for about four days, will become united, that it will "take" and acquire a good bloody supply of its own accord. What we do not yet know for sure is whether the old vessels are utilized or whether they degenerate and are replaced by ingrowth and development of new vascular sprouts from vessels in the graft bed. We also do not know what happens to the lymphatic channels and whether they also unite with sprouts from the lymphatic vascular channels in the bed.

In surgery on man skin grafting is necessary to make good a shortcoming of nature. When the full thickness of skin is lost or destroyed, it is never regenerated and so the best we can do is to produce a disfiguring and often function impairing scar,



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occasionally aggravated by keloid formation. However, some species of deer regenerate considerable areas of skin each year throughout life. The velvet that covers their growing antlers is skin in every sense of the word. If transplantation were to be applied to the study of skin neogeneses in antler formation, perhaps we may learn and exploit this knowledge to stimulate a latent regenerative potential in human skin.

The second category of problems relating to grafting is much more formidable. It arises from the incompatibility of homografts, that is those grafts exchanged between individuals of the same species who however are genetically dissimilar. After a transient period of functional well being that rarely exceeds a week or two homografts normally fail. However, autografts of the same tissue or organ are successful for long periods. This persistent state of intolerance of our bodies towards grafts derived from someone else is the barrier to successful transplantation in man and practically all other vertebrates.

Experimentalists can often circumvent the homograft barrier by employing animals of inbred genetically uniform strains. A similar genetic uniformity of course underlies the complete compatibility that identical twins display towards each other's grafts.

There are at least two instances where the immunological barrier is excepted. One is the natural homograft represented by the mammalian fetus. Another is the large proportion of corneal homografts which "take." The reasons why these are not rejected are as yet not fully understood.

L.H.N.

## **Safety Of Our Food Supply: Physiologically Significant Food Contaminants: I. Chemicals**

Contamination of foods by pathogenic microorganisms have forced public health agencies and the food industries themselves to develop suitable control measures. They have developed heat processing of canned goods, pasteurization of milk, refrigeration, meat inspection, and examination of food for filth. However, though significant progress has been made, the effectiveness of control measures is far from complete. Salmonellosis has increased greatly and the organisms have been detected in a wide assortment of foods particularly processed eggs, poultry, and swine.<sup>1</sup>

Then there are bacterial contaminants causing food poisoning by elaboration of toxic substances such as clostridium botulinum and toxin producing staphylococci. The clostridium still causes occasional outbreaks among humans in spite of strict precautions taken to avoid contamination of foods

by their toxins. It is much more common among animals and causes severe losses annually.

Intoxication by staphylococcus enterotoxin is probably the most common type of food poisoning in the United States. In a five year period 1957-1962 reported and unreported cases have been estimated to be in the hundreds of thousands. The Food Protection Committee of the National Academy of Sciences had this serious problem of food contamination by bacteria under serious study.

There is a second type of food contaminant significant to the public health, the non-nutrient chemical compounds capable of causing undesirable physiologic effects when ingested. These find their way into foods from several sources and have given rise to a diversity of problems necessitating continuing efforts to assure the safety of the food supply. Some are intentionally added to foods in the course of their production such as antioxidants, preservatives, coloring and flavoring agents, or even direct additions of nutrients themselves. Other chemicals knowingly introduced into foods are the residues of pesticides, herbicides used on plant crops, or residues of growth promoters used in animals. However, such additives are carefully controlled and are not considered to offer a serious hazard to health.

There is a large group of substances which Wogan<sup>2</sup> describes which inadvertently become components of food and some of them have been found to possess potent physiological effects. They may be termed unintentional contaminants. For example, one is chlorinated naphthalenes which contaminate processed animal feeds by lubricating oil used in the processing machinery. The disease so caused was called bovine hyperkeratosis which produced progressive damage to liver and other organs and death and produced enormous losses in animals. Another example of unintentional man-made food contamination is "Minamata disease" among persons in Japan. The cause was a mercury contaminated effluent from a large chemical manufacturing plant that emptied into the bay. The toxic agent accumulated in the tissues of fish and shellfish, thereby entering the food supply of the population and causing severe brain damage.

Then Wogan describes a disease "Chicken Edema," from a poison introduced into foods from sources wholly unrelated to the manufacture or processing of foods themselves but from a product derived in the course of industrial production of chlorinated compounds. The poison was in the fat component of animal feed and affected not only the chick but the rat, guinea pig, dog, and monkey. Fortunately, because all fatty acids destined for human consumption must be shown to be free of contamination, many were protected from this disease.



Then there is occasional contamination as a result of traditional or customary methods of food preparation. For example, in rural areas of Iceland the people preserve mutton and fish by a heavy smoking process and store them for long periods in functioning smoke houses. After such treatment they were found to contain significant quantities of 3.4 benzpyrene which produces malignant tumors when fed to rats. In human populations consuming substantial quantities over large periods of time, gastric cancer is the cause of one-third of all deaths. This is an unusual example of prolonged intake of large quantities of heavily contaminated foods.

The fact is that one can produce polynuclear hydrocarbons in charcoal broiling of steaks. Pyrolysis of melted fat drippings on the hot coals causes benz(a) pyrene to form—a known carcinogen which is present in concentration of 8  $\mu\text{g}/\text{Kg}$  of steak. Another example is represented by prolonged heating of fats and oils in such processes as deep-fat frying. Weakly toxic substances are formed which are co-carcinogens when fed chronically to rats.

These are all examples to illustrate the fact that some methods used traditionally in preservation and cooking of foods results in their contamination by biologically active compounds representing a further source of incidental contamination. We know almost nothing concerning the significance of this type of contamination during the usual home cooking operations.

L.H.N.

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## Infectious Resistance To Antibiotics

*"It appears that unless drastic measures are taken very soon, physicians may find themselves back to pre-antibiotic Middle Ages in the treatment of infectious diseases."* —Editorial, *New England Journal of Medicine*, 275: 277, 1966.

Emergent strains of antibiotic-resistant bacteria are threatening the dramatic healing power of antimicrobial agents. Until recently the principle mechanism that has been held responsible for this drug resistance was thought to be either spontaneous mutation, or normally existing resistant organisms which survived and multiplied as the non-resistant forms were killed by the antibiotic. We thought of this phenomenon as developing resistance to a particular drug and believed that it was a slow process at best.

However, in 1959 Japanese workers showed the development of resistance to multiple antibiotics in many strains of *Shigella*, not by mutations of new organisms but by transfer of such resistance from

resistant *shigella* to sensitive strains of *Escherichia coli* by conjugation of the two. This infectious multiple drug resistance is a process by which sets of genes determining resistance to several unrelated antibiotics are transferred together from resistant to sensitive strains by cell to cell contact.

These genes called R factor, are not located on the bacterial chromosome but on extra-chromosomal genetic elements which replicate autonomously and are composed of DNA. The R factor contains a region called resistance-transfer factor (RTF) that determines infectivity and to which the separate drug resistant genes are attached. The transfer of the R factor occurs not only within the species of enteric bacteria but also between groups as diverse as *shigella*, *salmonella*, *klebsiella*, *vibrio*, *pasteurella*, *serratia* and especially *Escherichia coli* which can and does serve as a reservoir since it facilitates transfer of the R factor from one pathogen to another and from animals to humans.

In staphylococci also, genes for resistance to penicillin, erythromycin, tetracycline, chloramphenicol and kanamycin are carried on extrachromosomal particles termed plasmids<sup>1</sup> and are transferred from cell to cell by phages. It may very well be that the rapid emergence of drug-resistance among staphylococci is related to dissemination of the plasmids by transduction with the aid of a phage.

Once the R factor was discovered in Japan it wasn't long before similar reports came from Great Britain in 1962<sup>2,3</sup> and by 1965<sup>4</sup> surveys of their distribution as well as studies of their fundamental properties were carried out in other European countries and Israel. In this country clinical studies of the R factor have just been reported by Kabins and Cohen from the Michael Reese Medical Center in Chicago.<sup>5</sup> They surveyed organisms recovered from patients with enterobacterial infections for transfer of resistance from organisms with the R factor to non-resistant organisms and found evidence for it in 13 cases. There were 72 strains of *shigella* isolated during the study. Of these 35 per cent were resistant to sulphadiazine, 25 per cent to streptomycin, 21 per cent to tetracycline and 1.4 per cent to chloramphenicol.

This contrasts sharply with the situation presenting as recently as 1962 when sulphonamide resistant *shigella* strains were not considered a major problem in the United States.<sup>6</sup> Kabins and Cohen's patients four years later showed multiple resistance transferred to 24 per cent of patients. It probably won't be long before strains will become resistant to chloramphenicol and ampicillin which are now the antibiotics of choice in typhoid and *salmonella* infections. Anderson and Lewis<sup>2</sup> have already pointed out how rapidly antibiotic resistance mediated by the R factor may be disseminated in *salmonella* strains.

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Neomycin and kanamycin are the antibiotics of choice in the treatment of epidemic diarrhea in infants. However, strains of *esch. coli* resistant to these agents have already been reported.<sup>7</sup> Thus the demonstration of transferrable resistance to these and other antibiotics in this group of organisms is of particular serious import. What is more alarming is that the administration of a single antibiotic to patients harboring sensitive shigellas has been followed in some cases by the excretion of multiple resistant strains of the same serotype.<sup>8</sup> Under the influence of antibiotics, resistant intestinal organisms initially present in small numbers multiply rapidly, become predominant flora and then transfer their resistance to any available pathogen. As a consequence of the prevalence of the R factor, the effectiveness of antibiotics in the treatment of enterobacterial infections may change virtually overnight.

Both Japanese and British studies have correlated the precipitous rise in frequency of the R factors with the increasing use of antibiotics not only in clinical practice but also in the care and feeding of livestock. Antibiotics are now incorporated routinely in livestock feeds, providing a constant selection pressure on R factors that can be readily transferred to man. Constant surveillance of the prevailing antibiotic sensitivity patterns both in the community at large and in the individual patient during the course of treatment will now be necessary to ensure the best results.

For the practitioners the immediate importance of infectious resistance is that it provides a mechanism for the rapid dissemination of inherited multiple antibiotic resistance between organisms of the same or different genera thereby posing a serious threat to effective treatment of enterobacterial diseases.

We can hope that the ingenuity of our basic scientists will produce new antibiotics to act against presently resistant organisms so that physicians will not be faced with the dire future of "finding themselves back to the pre-antibiotic Middle Ages in the treatment of infectious diseases."

L.H.N.

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## A Thymic Hormone Causing Lymphocyte Proliferation: Thymosin

In recent years much evidence has accumulated that the thymus gland plays a central role in the maturation, proliferation and immunological competence of the lymphocyte. Of the techniques employed to clarify the thymus role, two major types of observations imply that the influence is in part endocrine. The first is in vivo effects of thymic extracts on lymphopoiesis, lymphocytosis and immunological competence. The second is the effect of thymus grafts enclosed in cell-impermeable Millipore diffusion chambers in thymectomized animals.<sup>1</sup>

Previous attempts to isolate and purify a "thymic hormone" have been hampered by the lack of a satisfactory rapid assay method. The in vivo method previously described by Klein, Goldstein and White involves several inherent difficulties. One is the possible antigenicity of the extract which contains protein. A second difficulty is the limited number of fractions that can be tested in a given period of time and the testing of different fractions would have to be done in different animals, thereby unduly prolonging the assay of a given fraction. Then there is the deleterious influence of subclinical infection in mice which could mask the effect of any thymic fraction.

A new in-vivo method has now been described by Goldstein, Slater and White which permits the rapid assay of thymic fractions to as many as 20-30 per day. With this rapid assay method the preparation and partial purification of a thymus hormone which produces proliferation of lymphocytes has now been successfully achieved. It involves adding the various thymic fractions to be assayed directly to a lymphocyte suspension in-vitro and determining whether and how much H<sup>3</sup> thymidine is incorporated into DNA. If lymphocytes are not proliferating H<sup>3</sup> thymidine is not used up. Only when it is taken up is it evidence for DNA replication.

The technique then consists of adding H<sup>3</sup> thymidine and other labelled aminoacids that could be incorporated into DNA to a suspension of lymphocytes mixed with the thymic fraction. The



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DNA is then extracted and analyzed for the amount of label it has taken up. The amount of extract added determined the degree of  $H^3$  thymidine incorporation. At high concentrations the amount of stimulation of lymphocyte proliferation fell off. The scientists were astute to realize the possible presence of an inhibitory factor in the higher concentrations.

Pursuing the possibility further they soon obtained additional evidence in support of the existence of an inhibitory as well as a stimulatory substance in the thymic extract. By ingenious steps in the purification they found the extract was heat stable. In one fraction they found no activity in vitro until it was treated with acetone. However, it was active in vivo and this suggests that the fraction contained both a stimulator and inhibitor, the latter being inactivated in vivo. Once treated with acetone, the activator was isolated and separated from the inhibitor.

The in-vitro assay method has allowed an approximately 100 fold purification of the active principle by using ultra-centrifugation followed by a heat step and finally precipitation with cold acetone and gel filtration on P-10 polyacrylamide. This activity seems to be associated with a protein weight of around 4000-5000. Its activity is stable at 100°C but can be destroyed by incubation with trypsin.

Several other workers have reported various thymic fractions which could stimulate lymphocyte production, but they are all different from the present thymic hormone which is pure and identifiable, which acts in vitro and also in vivo.

The idea that an inhibitor is also present in thymic extracts as well as a stimulator of lymphocyte production is consistent with our knowledge of the balance between active and antagonistic hormones in the body. Insulin has its glucagon, parathormone, its thyrocalcitonin and now the lymphocyte stimulating factor, its inhibitor. As it stands now Goldstein, Slater, and White have prepared a purified cell free product which arises in the thymus, is transported via the blood to peripheral lymphoid structures where it stimulates lymphoid tissue proliferation. What the possible relationships may be between this thymic hormone and previously postulated thymic hormones and to immunological phenomena now awaits clarification.

Though somewhat premature we may be pardoned if we turn our thoughts to the possible practical outcomes of this new thymic hormone. There is a large body of evidence that the thymus has a fundamental role in host immunity. Furthermore lymphoid tissue is concerned with host immunity including antibody production. Would a substance that stimulates proliferation of lymphoid tissue contribute to promotion of host immunity. It prob-

ably would and it is not difficult to imagine how we could render many patients immune to repeated infections, or once infected, to contribute to their recovery. Can we hope to make a normal person supernormal in his resistance to infection by such a substance? Then there is of course the question whether the lymphocyte stimulating hormone is somehow involved in leukemia.

Another series of thoughts concerns inhibition of the hormone by a natural or synthetic substance. Would we contribute to suppression of host immunity and thus assist in achieving more significant successes than has been possible so far with immunosuppressive drugs. Doubtless these questions must be reverberating in the researchers' minds. Out of basic science contributions must come many practical applications, many as yet undreamed of.

L.H.N.

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### The Use Of Pronethalol In Overactive Beta-adrenergic Circulatory States

Frolich, et al<sup>1</sup> have succeeded with the use of propranolol in successfully treating two patients suffering from what they term the "hyperdynamic beta-adrenergic circulatory state." One of the patients was normotensive, a female aged 29, and the other also female, aged 39, was intermittently and mildly hypertensive. Both manifested palpitation, tachycardia and severe anxiety merely on sitting upright. Frohlich suspected that the symptoms were caused by exaggerated inotropic and contractile responses of myocardial beta-adrenergic receptors since the patients had no demonstrable heart disease. Their diagnosing and pin-pointing of the pathophysiology of the disorder is a classical example of clinical investigation of a high order.

Since the patients were asymptomatic in the supine position, the researchers reproduced all the symptoms by administering isoproterenol, a B-receptor stimulator. At once palpitation, tachycardia and anxiety resulted. A blockade of the B adrenergic receptors by pronethalol abolished the symptoms which also did not appear if the supine patient now assumed the upright posture. The conclusion seemed inescapable that these patients suffered from an overactive beta-adrenergic circulatory state since it could be abolished by B adrenergic inhibition.

The question of course immediately arose whether this state is primary or whether it is



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**Side Effects:** Overstimulation of the central nervous system, jitteriness and insomnia or drowsiness.

Dextro-amphetamine sulfate: Insomnia, excitability, and increased motor activity are common and ordinarily mild side effects. Confusion, anxiety, aggressiveness, increased libido, and hallucinations have also been observed, especially in mentally ill patients. Rebound fatigue and depression may follow central stimulation. Other effects may include dry mouth, anorexia, nausea, vomiting, diarrhea, and increased cardiovascular reactivity.

Meprobamate: Drowsiness may occur and can be associated with ataxia; the symptom can usually be controlled by decreasing the dose, or by concomitant administration of central stimulants. Allergic or idiosyncratic reactions: maculopapular rash, acute nonthrombocytopenic purpura with petechiae, ecchymoses, peripheral edema and fever, transient leukopenia. A case of fatal bullous dermatitis, following administration of meprobamate and prednisolone, has been reported. Hypersensitivity has produced fever, fainting spells, angioneurotic edema, bronchial spasms, hypotensive crises (1 fatal case), anuria, stomatitis, proctitis (1 case), anaphylaxis, agranulocytosis and thrombocytopenic purpura, and a fatal instance of aplastic anemia, but only when other drugs known to elicit these conditions were given concomitantly. Fast EEG activity, usually after excessive dosage. Impairment of visual accommodation. Massive overdosage may produce drowsiness lethargy, stupor, ataxia, coma, shock, vasomotor and respiratory collapse.



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caused by some more widespread autonomic imbalance. Could it perhaps be due to an inactive vagus? This was ruled out by normal responses to atropine and carotid sinus massage. Was it due to inadequate ganglionic transmission in the vagus system? They ruled this out by eliciting a normal reaction to trimethaphen camphorate. Could it be due to excessive quantities of catecholamines from a pheochromocytoma? This was ruled out by a negative phentolamine test.

Possible mechanisms further afield such as hyperthyroidism, porphyria, silent mitral stenosis, and psychoneurosis were all carefully considered and not found. In the end Frohlich and his co-workers were satisfied that these patients were suffering from a syndrome characterized by over-reactive B adrenergic receptors in the heart. Now that inhibition of these receptors is possible by pronethalol or guanethidine, the two patients suffering from a functionally crippling cardiac disorder were quickly relieved of this over-reactive sympathetic control of their hearts. The tachycardia, the dyspnoea and anxiety which was so prominent when the patients assumed an upright position before the blockade of the B receptors, no longer plagued these patients after receiving pronethalol.

The slowing of the heart rate and the subjective improvement effected by pronethalol makes us wonder what such a therapy would accomplish in patients which used to be termed neurocirculatory asthenia, who also had normal hearts but who suffered from palpitation, tachycardia, giddiness, sweating, dyspnoea and anxiety. These patients were recognized as far back as the civil war and termed soldier's hearts by Da Costa.<sup>2</sup> All early workers seemed to believe that anxiety underlay the symptoms and hoped that as anxiety decreased that "the symptoms would be given up." In fact, in the syndrome described above anxiety is a symptom, not a cause of the disorder.

Before we knew about the beta-adrenergic receptors and before we had a pharmacologic agent in pronethalol to antagonize them, the mechanism of origin of neurocirculatory asthenia was of course not understood. It had been suspected that an "imbalance" of the autonomic nervous system was responsible for the severe reactions which followed slight provocations in a "normal" heart. All workers sought for infection, physical exhaustion, nervous prostration, or anxiety for the cause of the symptoms which seemed out of proportion to any recognized organic cause.

Ordinarily the heart rate is precisely adjusted by balancing the retarding effects of vagal discharge against accelerating effects of sympathetic stimulation. This is a form of reciprocal innervation at the effector organ, the sino-atrial node. In addition reciprocal innervation is also prominent in the

central control over heart rate, i.e. at the medullary center. Here the neural connections are so organized that activation of the motor nucleus of the vagus is associated with simultaneous inhibition of the medullary acceleration center and vice-versa.

Evidently Frohlich's patients showed the balance thrown to favor over-activity of the beta-adrenergic control. If we look carefully we will probably find also the opposite type of patient in whom the autonomic balance might be in favor of over-active vagus control. The older physicians in fact recognized both sympathotonic and vagotonic types.

We are still without knowledge as to why patients suffer from the "hyperdynamic beta-adrenergic circulatory state." But such patients do occur and the beta-adrenergic blocking agents will now emerge as a useful tool to test for the existence of this state as well as a therapeutic agent for its control. These agents have also been found useful in tachycardias of diverse origin, angina pectoris, more recently also in hypertrophic obstructive cardiomyopathies,<sup>3</sup> in which over-activity of the beta-adrenergic receptors seem to be a prominent feature and in arrhythmias found in digitalis intoxication.<sup>4</sup>

L.H.N.

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## Isuprel In Amniotic Fluid Embolism

It is important for the internist as well as the obstetrician to be familiar with amniotic fluid embolism since the internist is often called to the delivery room when cardiopulmonary problems develop. The syndrome deserves wider recognition as an emergency which may suddenly confront the internist who is hastily summoned to the obstetrical department to see a patient with sudden onset of dyspnoea or shock. Amniotic fluid embolism is probably much more frequent than the number of previously reported cases would indicate. Cases previously called "obstetrical shock" and pitressin shock may actually have been cases of pulmonary embolism. It is probably the most common cause of unexplained shock occurring on the delivery table.



When autopsied cases are collected and compared the syndrome is remarkably uniform. The patient may be in her early 30's, a multipara in whom the prenatal course has been uneventful. Labor, however, is often tumultuous. During labor or within an hour of two following delivery, there suddenly appears acutely developing anxiety, dyspnoea and shock without chest pain, without a previous history of heart disease, and without evidence of significant hemorrhage to explain this state. Diffuse rales and other evidence of acute pulmonary edema may be present. Coma, death from anoxia and circulatory collapse may then occur within minutes of the onset of symptoms or after an interval of several hours. In short, there is the clinical picture of shock and dyspnoea out of proportion to the degree of hemorrhage in a person who had no heart disease prior to the onset of severe signs of right heart failure and dyspnoea and no sign of thrombophlebitis. It is, of course, a classical picture of pulmonary embolism.

Non-fatal cases have been described but nearly all cases reported have ended fatally and this has permitted the establishment of the correct diagnosis. The case described by Nichols<sup>1</sup> did survive and recover completely and serves to illustrate the natural history of amniotic fluid embolism and the setting in which it occurs. The fact that non-fatal cases also occur makes it probable that the incidence of this disorder is distinctly higher than hitherto supposed. Perhaps this may account for variability in the reported incidence from 11 in 37,000 live births to 1 in 400. However, even though cardio-respiratory deaths are not uncommon, a cause of it, amniotic fluid embolism, is not discussed or listed in standard textbooks of medicine and Nichols points out that one large text on obstetrical complications fails to mention the subject.

The exact physiological mechanism of amniotic fluid embolism is unknown. Normally almost no amniotic fluid escapes into the maternal circulation. With radio-isotope techniques it has been demonstrated that amniotic fluid and particulate matter it sometimes contains may enter the uterine veins causing pulmonary embolism in the mother and maternal deaths. Intravenous injection of unfiltered amniotic fluid has reproduced this syndrome in experimental animals, whereas injection of filtered amniotic fluid is not followed by this syndrome. Clearly a variable amount of fluid debris is responsible and the speed of death or recovery must depend on the amount which has entered the venous circulation and obstructed the pulmonary circulation.

At post-mortem meconium and other amniotic fluid constituents are found in the pulmonary ves-

sels of the mother, epithelial cells, lanugo hairs, mucin, bile and fat in small amounts. The findings of these constituents in the small pulmonary vessels is the pathologist's main diagnostic criterion. What causes the crisis in the fetus that results in expulsion into the amniotic fluid of the particulate matter needs to be discovered and avoided. What leads to the entrance of such fluid into the mother's venous system also remains to be explained. Once it enters, however, it obstructs the pulmonary circulation and also has the effect of tissue thromboplastin so that hypofibrinogenemia with uterine or generalized bleeding may develop if the patient survives beyond the first three hours.

A wide variety of procedures have been used in the treatment of this alarming complication such as O<sub>2</sub>, morphine, intravenous fluids, corticosteroids, vasopressor agents, digitalis, positive pressure breathing, and even venesection, but none have been shown to be critical in the treatment of amniotic fluid embolism. Only one method of treatment proposed so far has shown any real promise although it has been applied only in animals, but in whom the results were strikingly curative.

From the University of Sidney, Australia, Halmagyi, et al<sup>2</sup> have reported a study of cardio-respiratory dynamics in a small number of sheep. In these animals the intravenous infusion of unfiltered human amniotic fluid was regularly followed by signs of pulmonary embolism: pulmonary hypertension a severe fall in lung compliance and arterial hypoxia. With equal regularity all these consequences of amniotic fluid embolism were prevented or, once started, were abolished by administration of isoproterenol used either as an aerosol or as an intravenous infusion.

Dr. Halmagyi points out that isuprel has been employed clinically in treating thrombotic pulmonary embolism and advises that this drug should be used preferably subcutaneously in a dose of 2 mg reserving intravenous administration for the extreme case requiring resuscitation. Obviously if hemorrhage from hypofibrinogenemia supervenes, then heparin will also be required.

Now that experimental data shows that amniotic fluid embolism in experimental animals can be consistently prevented or cured, we have an especially great need for diagnosing the condition in obstetrics and instituting correct therapy.<sup>3,4</sup> Obviously if isuprel works in one type of pulmonary embolism we should not forget its trial in other forms of pulmonary embolism threatening life.

L.H.N.

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have an adverse effect on pregnancy, the safety of their use on pregnant females has not absolutely been established. Therefore, they should not be used extensively on pregnant patients, in large amounts, or for prolonged periods of time. 2. *Occlusive dressing method*—With occlusion of extensive areas, systemic absorption of the corticosteroid may occur, and suitable precautions should be taken. Occasional patients may show contact sensitivity to a particular dressing material or adhesive. Miliaria, folliculitis, and pyoderma have been seen infrequently with the use of this technique. The development of infection requires appropriate antibacterial therapy and discontinuation of the occlusive dressing method. Local atrophy and striae have been reported with protracted occlusive dressing therapy. While lesions relapses can be expected to occur in many psoriatic patients, remission may persist for several weeks to several months in favorable cases. The patient whose psoriasis is in an active stage, with recent appearance of new lesions, may not be a good candidate and may show early relapse. Some plastic films may be flammable, and due care should be exercised in the use. Similarly, caution should be employed when such films are used on children to avoid the possibility of accidental suffocation. **Side Effects:** Side effects are not ordinarily encountered with topically applied corticosteroids. As with all drugs, however, a few patients may react unfavorably to Synalar under certain conditions. **References:** 1. Cahn, M. M., and Levy, E. J.: *J New Drugs* 1:262 (Nov.-Dec.) 1961. 2. Meenan, F. O.: *J Iris Med Ass* 52:75 (Mar.) 1963. 3. Robinson, H. M., Jr., Raskin, J., and Dunseath, W. J. R.: *Southern Med J* 56:797 (Jul.) 1963.



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## Estrogen And The Aging Process

All living organisms begin to age soon after conception. If we knew what factors influence and accelerate the progression of the aging process it should be possible to counteract at least some of them. We all believe the human body is capable of remaining youthful longer than it usually does. Apparently women tend to age much more rapidly after the menopause than they do before. It is possible for an aging woman to retain her health, vigor and enthusiasm for living even after the climacteric.

This problem has long held the interest of members of the Department of Obstetrics and Gynecology of the University of Chicago.<sup>1</sup> For more than twenty years they have been accumulating data on the long term administration of estrogen to patients lacking functioning ovaries either as a result of menopausal changes or castration. They have assembled impressive evidence of the part estrogen can play in preventing certain manifestations of the aging process in women.

The early patients in their study were women who had had their ovaries removed at hysterectomy. A few days after operation they were given estrogen (at that time diethylstilbestrol) to suppress the onset of the climacteric. The menopause did not appear, the patients retained their well-being and it was this observation which provided the stimulus for the investigators and for the patients to continue under observation with periodic examinations.

To the group of castrates receiving replacement therapy, were added three additional groups: women in the natural menopause period as controls, castrated women who received no hormonal therapy, and women who had had a natural menopause and no hormonal medication. In the first years of their study the experience paralleled that of other investigators. The menopausal syndrome as well as the subsequent atrophic changes that eventually affect not only the ovaries, but indeed the entire body of women without functioning ovaries was quite responsive to supplemental estro-

gens. When continued indefinitely such treatment abolished the disturbing menopausal symptoms and prevented or delayed the development of atrophic changes in the vagina, breasts and skin.

One important question has been whether estrogen replacement can retard the development of atherosclerosis in post-menopausal women. It has long been recognized that after the menopause, women rapidly develop arterial changes so that in the fifth to the seventh decade of life the incidence of atherosclerosis begins to approximate that found in men of similar ages.<sup>2,3</sup> It is this growing interest in the relation between absence of estrogen and the development of atherosclerotic disease which sparked another phase in Davis, et al's study. They initiated a program of intensive examination of their patients on estrogen replacement therapy at regular intervals. Included in the examination were determinations of serum lipids, cholesterol-phospholipids and in recent years fatty acids and triglycerides.

Like other investigators<sup>2</sup> they found that women with functioning ovaries were protected against atherosclerosis and its sequelae. What was especially significant was that administration of estrogen after the menopause tended to prolong this protection indefinitely. A final dimension was added to the study when they attempted to determine what if any was the relationship between estrogen and osteoporosis. This relationship is not so well understood as is that between gonadal failure, atrophic changes and atherosclerotic disease.

The rate of bone formation is controlled by the extent to which osteoblasts are stimulated by stresses and strains and also by estrogens and androgens. In the normal adult skeleton the rate of bone formation is matched by the rate of bone resorption. Lutwak and Whedon<sup>4</sup> have estimated that currently at least four million persons in the United States have a significant degree of osteoporosis and that four-fifths of these patients are post-menopausal women.

Post-menopausal osteoporosis is a physical change, an aging phenomenon, not a disease. It is the most common metabolic disorder of bone, representing a decrease in total bone mass with no change in its chemical composition. As far back as 1941 Albright<sup>5</sup> suggested that osteoporosis is a condition with too little bone matrix and postulated that it was brought about by inadequate concentration of estrogens. Decreased activity of the aging female reduces the stress and strain stimulus to bone formation. The results are a disproportion between the decreased rate of bone formation and the normal rate of absorption with gradual de-



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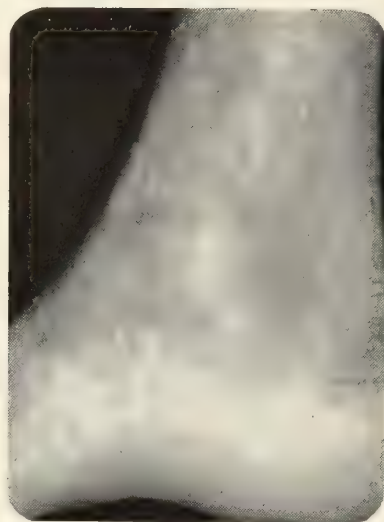
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crease in bone mass. This reduction of stress and strain as well as disappearance of estrogen renders the female much more susceptible to development of osteoporosis. In men too, decreased physical activity as senility approaches, helps to bring on osteoporosis. However, before senility, men are spared much of the process of decreasing bone mass since their gonads continue to produce androgens for most of their lives.

This interpretation of the pathogenesis of post-menopausal osteoporosis, i.e., loss of estrogens and reduced physical activity, has been confirmed by Wallach and Hinman who summarized their 25 years of experience with 242 post-menopausal women, prior to and following the administration of estrogens. They concluded that the continuing height loss of their patients was a sensitive indicator of the advance of osteoporotic processes and that following the administration of estrogens to their subjects further height loss ceased.

Davis, et al<sup>1</sup> have perfected and applied a new and single instrumentation which has made it possible to evaluate bone changes easily and accurately in serial and survey studies.<sup>6,7,8</sup> They determined the degree of osteoporosis by the transmission of low energy radiation from I<sup>125</sup> through in-vivo bone samples. The measure used was the linear absorption coefficient of overall bone of a phalanx. Their results also show that post-menopausal osteoporosis is prevented or retarded by estrogen replacement therapy as compared with a control group that did not receive estrogens. Patients without hormone supplement showed a sharp drop at the 5-10 year interval in mineral content of bone with a slower decline later. The patients with additional hormone showed almost no decrease in mineral bone content for the first 5-10 years and only a slow decline in the next 10-15 years but never approximating the non-treated group.

Current practice in medical management of the menopause to prescribe supplementary estrogens only for relieving the symptoms is clearly archaic. We see that the ovarian failure and the drop in the supply of estrogens initiated widespread atrophic changes which begin in the reproductive organs but do not stop there but extend rapidly to the body tissues and bony skeleton. Furthermore, this general aging is associated with the progress and development of atherosclerotic disease and its dire sequelae.

At present our philosophy is to relieve the woman's symptoms by providing her with estrogen to supplement her failing ovarian supply during the establishment of her climacteric. As we have seen above long term estrogen substitution for com-

plete gonadal failure is far more rewarding and should be continued indefinitely. It should help women to retain their good health in their advancing years. It should add quality to their lives.

L.H.N.

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## Precautions In The Use Of Diuretic Agents In The Treatment Of Hypertension

A very important recent development in medical pharmacology has been the use of diuretic agents in the treatment of hypertensive disease. These agents increase renal excretion of salt and water. In fact, it has been generally accepted that reduction in dietary salt intake is essential in anti hypertensive therapy. Whether dietary chloride is implicated in the pathogenesis of hypertension is not really important because one can accomplish hypotensive reactions to dietary sodium restriction alone.

Rigid oral sodium restriction does indeed reduce blood pressure but this therapeutic regimen is unacceptable to patients and as a result it is almost never used anymore now that we have the benzo-thiadiazine diuretics.

During the past several years many congeners have been devised as a result of altering the structure of chlorothiazide so that we think of them as belonging to the thiazide diuretic group. They may

all be used interchangeably. When used in maximum dosage they have equivalent effects on both the excretion of sodium and blood pressure reduction and no single one of them is superior to any of the others. They may all produce the potassium depletion following prolonged administration. They may all reduce carbohydrate tolerance, perhaps by virtue of lowering serum potassium, and they may all elevate the serum uric acid and even precipitate gout.

The mechanism of action of the hypotensive effect of these drugs is unknown at the present time. It is possible that a reduction in plasma volume and cardiac output may be responsible for the initially observed moderate hypotensive effect. However we know that the hypotensive effect persists despite re-expansion of the blood volume. One idea is that digital blood vessels which are hyper-reactive during hypertension become less responsive to vasopressors after the thiazides. It may also be that the decreased responsiveness of the vascular smooth muscle is caused by altered sodium ion gradients.

Spironolactone (aldactone) inhibits the effects of aldosterone and DOCA, produces increased sodium excretion, reduced potassium excretion, and also hypotension, especially in patients on a restricted sodium intake. In general the effects of spironolactone parallel those of the chlorothiazide diuretics with the exception of the serum potassium which does not decline and may be slightly increased.<sup>1</sup> When compared to the thiazides and mercurial diuretics the natriuretic effect of spironolactone is comparatively slight but the hypotensive action is comparable in magnitude with that of the thiazides.

We thus have two broad categories of drugs which are efficacious by themselves in the treatment of hypertension, the benzothiadiazines and the spironolactones. The hypotensive effectiveness of the aldosterone antagonists is as great as that of the thiazides, but are without the side effects seen with increasing frequency in connection with prolonged use of the thiazides. Since hypertension is a long chronic condition, we have to be prepared for treating a patient with hypertension for many years.

The important point then is that we have to be prepared to continue treatment for a decade or more. And so it is necessary to consider not only the effects of any hypotensive agent upon the blood pressure, but the side effects upon other bodily structures and functions. We are seeing many side effects and these have to be taken into consideration because it is theoretically possible that side effects from a compound given over many years

may themselves have a significant effect on the morbidity and mortality.

We are not entirely sure that a lower blood pressure is the direct cause of a longer life span. However there is a lot of evidence that if you do lower arterial pressure beneficial effects will occur provided of course the side effects do not counteract the potential good effect. We must always remember that it is not just the blood pressure we are treating but the total individual. One major problem in hypertensive disease is atherosclerosis and coronary artery disease. This is the main cause of death in the hypertensive population. If there is anything in the treatment of hypertension which will tend to promote arterial degeneration then we must re-evaluate the drugs from this point of view.

We think we can identify factors that increase the risk of coronary artery disease. Diabetes or hyperglycemia increases the risk of coronary artery disease. Hyperuricemia and gout are also significant risk factors. It is obvious then that from a theoretical point of view it is desirable to use drugs in treating hypertension, that do not have any of these side effects.

We must recognize that though well tolerated the thiazides do have untoward side effects depending to some extent upon the dosage employed and the length of time they are being taken. Untoward effects include drug rash, dehydration, hyponatremia, hypokalemia, hypochloremic alkalosis, nitrogen retention, hyperglycemia, hyperuricemia, gout and, in fact, digitalis intoxication promoted by hypokalemia.

Hollander<sup>2</sup> points out that hypokalemia occurs in about one-third of patients receiving diuretic drugs. It is usually asymptomatic. Nevertheless, every patient who develops hypokalemia has an important defect of total body potassium usually about 15-20 per cent below normal,<sup>3</sup> in chronic long-term therapy. These people may be non-edematous, active up and about and eating, but often with weakness, vague and indescribable feelings. Although such patients are usually asymptomatic, not infrequently if they are on digitalis, signs of toxicity gradually develop.

Hollander's view is that the diuretics are capable of aggravating or precipitating diabetes in patients with abnormal glucose tolerance tests or who have a positive family history of diabetes. The results of glucose tolerance tests indicate that the thiazide and other diuretics increase significantly the fasting blood sugar levels of diabetics but not of non-diabetics. But they can cause a significant increase of the two-hour blood sugar after an oral glucose load in non-diabetic as well as diabetic hypertensive patients. This may be due in part to hypo-



# MOLECULAR REMODELING—

## *laboratory exercise or clinical necessity?*

More than twenty-five years have passed since the discovery of the diuretic activity of sulfanilamide started pharmacologists on a succession of molecular remodelings to find the ideal diuretic.

### **Diuresis—a sought-after clinical effect from an unwanted side effect**

It started in 1937 when a clinician reported that the administration of a sulfonamide was sometimes accompanied by an unexplainable side effect—metabolic acidosis.<sup>1</sup> Three years later the side effect was explained. The sulfonamide radical of sulfanilamide inhibited carbonic anhydrase,<sup>2</sup> the enzyme responsible for converting carbon dioxide and water to hydrogen ions and bicarbonate ions.

Later, other investigators showed by dog experiments that metabolic acidosis probably resulted when the inhibition of carbonic anhydrase upset the exchange of hydrogen and sodium ions, causing increased excretion of sodium as the bicarbonate.<sup>3</sup>

It was twelve long years after the first report of the unexplainable side effect (metabolic acidosis) that it was finally shown that large doses of sulfanilamide administered to edematous patients were indeed capable of promoting diuresis.<sup>4</sup> However, the possibility of toxic effects from its prolonged use and its relatively weak diuretic action made it impractical for clinical use as a diuretic.<sup>5</sup>

Because the inhibition of carbonic anhydrase seemed to be the key to effective diuresis, investigators began to look for more potent enzyme inhibitors—in the hopes that they would be more effective diuretics.

The most important of these early compounds, acetazolamide, enjoyed several years of fairly wide clinical use.

Its carbonic anhydrase inhibitory activity was several hundred times greater than that of sulfanilamide.<sup>6</sup> The increase in inhibitory activity, however, increased not only the excretion of sodium and bicarbonate ions, but also the excretion of potassium.<sup>7</sup> And, like its predecessor, acetazolamide precipitated mild acidosis. Its prolonged use could result in hypokalemic acidosis.<sup>7</sup>

### **The 'thiazides'—an answer to the metabolic acidosis caused by carbonic anhydrase inhibition**

Despite the fact that the sulfonamide

group appeared to be responsible for carbonic anhydrase inhibition which in turn appeared to be responsible for diuresis, investigators began to synthesize compounds with structural alterations to the sulfonamide group.

The first major breakthrough came with the synthesis of chlorothiazide. Altering the sulfonamide group did indeed alter the ability of chlorothiazide to inhibit carbonic anhydrase—it was only 1/10th as potent as acetazolamide in inhibiting the enzyme.<sup>8</sup> Despite the drop in inhibitory potency, however, chlorothiazide proved to be an effective diuretic—an observation that led to the conclusion that its diuretic action was due to some mechanism other than its action on carbonic anhydrase.<sup>9,10</sup>

For effective diuresis, chlorothiazide was administered in daily dosages ranging from 250 to 2000 mg.<sup>11</sup> It increased the excretion of sodium and chloride; and, to a lesser extent, potassium and bicarbonate.<sup>11</sup> The excretion of potassium appeared to be maximal at higher dose levels at which, theoretically, the carbonic anhydrase inhibitory effect is more active.<sup>11</sup> Its prolonged use, therefore, could sometimes result in metabolic hypokalemic, hypochloremic alkalosis.<sup>7</sup>

### **Naturetin—effective diuresis with more favorable electrolyte balance**

Other thiazides followed—with improvements being aimed at two particular areas: 1. attempts to increase diuretic action in relation to the milligram potency of the drug, and 2. attempts at a more favorable sodium/potassium ratio in the urine, i.e., to decrease the excretion of potassium while maintaining the excretion of sodium.<sup>12</sup>

One of these, Naturetin, Squibb Bendroflumethiazide, has made advances on both these points. "By adding a 3-benzyl radical to hydroflumethiazide a rather dramatic reduction in dose range is accomplished. With this drug, effective sodium excretion is obtained with

doses between 2.5 and 10 mg., which is a 200 to 1 ratio as compared to chlorothiazide..."<sup>13</sup>

Moreover, due probably to its virtual lack of carbonic anhydrase inhibition, Naturetin (bendroflumethiazide) has been shown to cause less potassium and bicarbonate loss and less alteration in urinary pH than either chlorothiazide or hydrochlorothiazide.

Naturetin is outstandingly effective not only in establishing, but also in maintaining, excretion of retained fluid in edematous patients. And its duration of action is sufficiently prolonged to allow a single daily administration in most patients. Naturetin is also an effective antihypertensive agent.

**Contraindications:** Severe renal impairment; previous hypersensitivity.

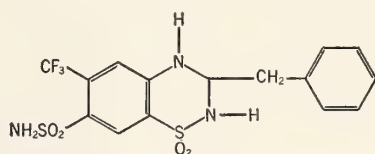
**Warning:** Ulcerative small bowel lesions have occurred with potassium-containing thiazide preparations or with enteric-coated potassium salts supplementally. Stop medication if abdominal pain, distension, nausea, vomiting, or G.I. bleeding occur.

**Precautions:** The dosage of ganglionic blocking agents, veratrum, or hydralazine when used concomitantly must be reduced by at least 50% to avoid orthostatic hypotension. Electrolyte disturbances are possible in cirrhotic or digitalized patients.

**Side Effects:** Bendroflumethiazide may cause increases in serum uric acid, unmask diabetes, increase glycemias and glycosuria in diabetic patients and may cause hypochloremic alkalosis, hypokalemia; cramps, pruritus, paresthesias, and rashes may occur.

**Supplied:** Naturetin (Squibb Bendroflumethiazide) 5 mg. and 2.5 mg. tablets. Also available Naturetin c K [Squibb Bendroflumethiazide (5 or 2.5 mg.) with Potassium Chloride (500 mg.)]. For full information, see Product Brief.

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kalemia which seriously impairs insulin production.<sup>4</sup> Fortunately the hypoglycemia appears to be reversible after withdrawal of the diuretics.

The incidence of acute gouty arthritis during diuretic therapy appears to be increasing and is estimated to occur in about 10 per cent of our patients receiving diuretic therapy. In fact these compounds produce a significant elevation of serum uric acid in hypertensive patients who do not show manifest gout. However, in Hollander's patients onset of gouty arthritis occurred on an average of 3.7 years after the start of thiazide therapy ranging from eight months to seven years. All gouty patients responded to colchicine and probenecid and the arthritis subsided after withdrawing the thiazide diuretic.

It is clear from what has been said that the thiazide diuretics may not be used indefinitely but intermittently. What then can be used in the interval periods to continue hypotensive therapy and what should be used concurrently with them to avoid the electrolyte disturbances that occur so frequently after their prolonged use.<sup>5</sup>

Hollander suggests using spironolactone (aldactone) 25 mg. three times a day with the thiazides and also when the thiazides need to be discontinued. When used with the thiazides the aldosterone antagonist counteracts the potassium wasting effect of the thiazides and also augments the hypotensive and diuretic effects. It is also more effective and much better tolerated than potassium supplement in the treatment of hypokalemia. Of course before instituting aldactone therapy one must know whether the serum potassium level is already too high as occurs in some patients with late renal disease.

It would appear that spironolactone (aldactone) will come to occupy an important place in the treatment of hypertension, by itself as well as in conjunction with the thiazides.<sup>6</sup>

L.H.N.

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## Tests For Atherophilia

Some people develop myocardial infarction and others don't. It is only logical to take those who have recovered from an acute infarct and try to define the special characteristics which set such patients apart from the general population. Since there are hereditary, anthropomorphic, and metabolic parameters associated with the development of coronary artery disease (CAD) both in prospective and retrospective and cross-sectional studies,<sup>1</sup> the findings in the two types of studies has permitted the conclusion that the incriminated characteristics are present before the onset of overt complications of atherosclerosis supervene. Out of such thinking has developed the concepts of identifiable risk factors that contribute to CAD as well as the additivity of their influences.

Several of these factors appear with substantial frequency and magnitude in the populations of most of the developed countries of the world. One may assume that taken in combination these factors can provide a fairly accurate index for the individual of the risk of developing CAD. Hatch and his associates<sup>2</sup> believe that no preventive regimen can be applied until these peculiarities of the "coronary prone" individual are known. It may of course be that even then preventable measures might be impractical.

What Hatch and his associates have done is to compare by a battery of metabolic tests 24 young men who survived an acute myocardial infarction with 20 age-matched healthy subjects—10 business and professional men and 10 prisoners. Analysis of the data gave evidence in varying degrees of an abnormal metabolic state manifested principally by impaired glucose tolerance and hyperlipidemia. Such positive findings heavily infiltrated the patient series, while they were sparsely scattered among the controls. In the prisoners especially was there a low serum cholesterol and relative freedom from CAD. It is significant that many of Hatch's coronary victims "maintained the eating habits of a robust early manhood after caloric and nutrient requirements had declined sharply."

Thus overweight, overnutrition, and cigarettes appear once again to be the menaces to the man with the vulnerable genetic constitution. Dietary fats and sugars are in particular disrepute. The authors view is that atherosclerosis and CAD are accelerated by a variety of environmental factors which exert their actions at least in part upon the genotype of the individual (see figure on front cover). Because of the many factors which additively lead to vascular disease, Hatch's report says "a simple pathogenesis for atherosclerosis and myocardial infarction, such as the consumption of too



much fat or cholesterol or sugar — will not be found.”

In Hatch's study over a dozen laboratory determinations were made in each case. Undoubtedly research of this type will help us to recognize the pattern of susceptibility to overt ischemic heart disease. The question arises how many metabolic tests at present are necessary. When in the lifetime of an individual should such testing begin. Will we ever come to a specific test for atherophilia which Sprague<sup>3</sup> calls the “Damocles test.” Fortunately no such test is presently available to separate the boy baby as one over whose head hangs the scimitar of CAD. It would cause too much unhappiness to parents and child alike.

Work such as Hatch's and his group suggests that it might just be possible that not smoking cigarettes and keeping one's weight at that of age 25 would prevent much of the atheromatosis and that is all we need to be told. This is really, however, a very old story. Hippocrates thought weight control a good idea almost 2,000 years ago and so did Celsus. The life insurance companies have known this for over a generation. It has been shown that the almost inevitable fate of the American male is to gain weight during middle age. Reversal of this pattern would probably prolong many lives.

What is further important is that individuals who exhibit many of the criteria indicative of increased risk are not uncommon in our population. Their identification as candidates for CAD disease early in life is now possible and poses a significant medical and public health problem.

(See cover story page 763).

L.H.N.

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## Nocturnal Or Recumbency Muscle Cramps

Quinine Sulfate USP, either alone or in combination with aminophylline or other drugs has been used for many years in the treatment of nocturnal or recumbency cramps, though no controlled trials supporting the effectiveness of this therapy have been reported.

What happens in the muscle, the nervous system, or the metabolic pathways to precipitate recumbency cramps is not known. Unlike intermittent claudication, which occurs during exercise in per-

sons with inadequate arterial circulation, recumbency cramps do not occur during exercise and are independent of arterial circulation. The cramps are often precipitated by stretching or extension of the legs and feet, as during rest or in light sleep. Walking or bending the feet backward sometimes gives relief. There is no evidence supporting the belief that the cramps are caused by a temporary loss or depletion of calcium, sodium or any other mineral or nutrient.

*Quinine Therapy* — In experimental studies, quinine has been found to decrease the excitability of the motor end-plate region of muscle, with reduction of response to repetitive nerve stimulation. The drug has also been found to act directly on the muscle fibers by increasing the refractory period, thus diminishing response to tetanic stimulation. The trial of quinine sulfate for night cramps followed a report by F. Kennedy and A. Wolf (*Arch. Neurol. Psychiat.*, 37:68, 1937) that it was successful in relieving muscle spasm in myotonia congenita.

Reasoning that a drug effective against one type of muscle spasm might work against others, H. K. Moss and L. G. Herrmann gave quinine sulfate to 15 patients with night cramps, with almost 100 per cent successful results (*JAMA*, 115: 1358, 1940). A. Gootnick (*Arch. Intern. Med.*, 71:555, 1943) reported that in 28 of 30 patients, including several who had not had a cramp-free night in months, the administration of quinine sulfate in a dose of 3 grains, (200 mg) at bedtime abolished the spasms. This, too, was an uncontrolled trial, and the author noted that in several instances, discontinuance of the quinine after three days was not followed by re-appearance of the cramps; some patients remained free of cramps a week or more, and some indefinitely. A number of other trials have been reported since then, all of them uncontrolled.

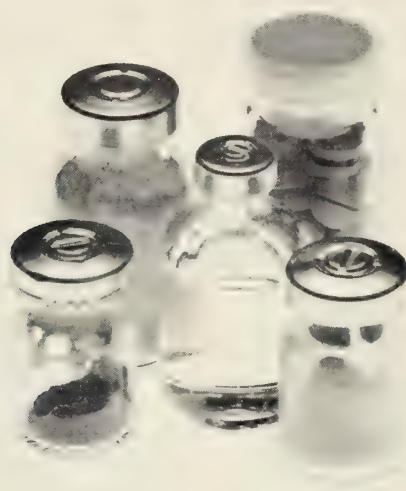
Besides quinine sulfate, drugs claimed at one time or another to be effective against nocturnal cramps include Aminophylline Tablets USP, calcium salts, and antihistamines. None of the claims have been confirmed by controlled trials, and the recent evidence supporting them is even less convincing than that for quinine. Before any trial of drugs it is important to distinguish recumbency cramps from myotonia, the slow relaxation of myxedema, hypocalcemic tetany and the contracture of phosphorylase deficiency.

*Conclusion* — Notwithstanding the favorable experience of many physicians with quinine sulfate, controlled trials reliably evaluating its effectiveness in preventing the occurrence of nocturnal or recumbency cramps and establishing optimum dosage are very much needed.

*Reprinted from The Medical Letter on Drugs and Therapeutics, New York, N.Y., Vol. 8, No. 20, October 7, 1966.*

against the usual gram-negative urinary pathogens

## Why use five...where **one** will do?



**In a recent 217-patient hospital study,<sup>1</sup>** urinary tract infections were treated with a variety of widely prescribed antimicrobial agents including: a sulfonamide (40 patients), chloramphenicol (20 patients), nitrofurantoin (33 patients), nalidixic acid (30 patients), tetracycline (27 patients), colistimethate sodium (22 patients) ... and 2 combinations of 5 agents each (45 patients). The 2 combinations were selected to afford maximal theoretical antibacterial coverage against the usual urinary pathogens. They were (1) tetracycline, chloramphenicol, nitrofurantoin, ristocetin and polymyxin B; and (2) tetracycline, chloramphenicol, erythromycin, nitrofurantoin and colistimethate sodium.

**This clinical study shows** that the two combinations of antibiotics were not superior to some of their single components. The authors point out that antibiotic antagonism often negates theoretical advantages of multiple therapy. Coly-Mycin Injectable (colistimethate sodium) was one of the single components that was shown to be equal to the combinations and eradicated bacteriuria in two-thirds of the patients.

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1. McCabe, W. R., and Jackson, G. G.: New England J. Med. 272:1037, 1965.



in gram-negative urinary tract infections often the single well-chosen agent



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**Adverse Reactions:** Occasional reactions such as circumoral paresthesias, tingling of the extremities, pruritus, vertigo or dizziness may occur. Reduction of dosage may alleviate symptoms. Therapy need not be discontinued, but such patients should be observed with extra care.

**Warning:** Patients should be cautioned not to drive vehicles or use hazardous machinery while on therapy.

**Precautions:** In cases of impaired or suspected renal impairment, use with greater caution and reduce dosage in proportion to extent of impairment. Transient elevations of BUN have been reported. As a routine precaution, appropriate blood studies should, therefore, be made during prolonged therapy.

As with all polypeptides, the possibility of muscular weakness, including apnea, due to inadvertent overdosage or normal dosage in the presence of impaired renal function, should not be overlooked. In cases of apnea, medication should be promptly discontinued and assisted respiration given until serum levels fall and normal breathing is restored.

Other antibiotics, such as kanamycin, streptomycin, dihydrostreptomycin, polymyxin, and neomycin, may also have varying neurotoxic or nephrotoxic potential. They should be used with great caution concomitantly with Coly-Mycin Injectable (colistimethate sodium).

**For deep intramuscular injection only.**

**Dosage:** By the I.M. route only, in 2 to 4 divided doses ranging from 1.5 to 5 mg./Kg./day (0.7 mg. to 2.3 mg./lb./day). Average adult dose is 2.5 mg./Kg./day (1.1 mg./lb./day). In the presence of bacteremia, septicemia, or other serious infection, greater than average doses may be required; however, maximum daily doses should not exceed 5 mg./Kg. (2.3 mg./lb.) where renal function is normal.

**Not recommended against *Proteus*.**

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# Hearing Aid Selection And Usage In Young Hearing-Impaired Children

Mark Ross, Ph.D., and Jay W. Lerman, Ph.D.

■ In a previous article<sup>3</sup> the importance of early detection of hearing loss in children was stressed. The conclusion was drawn that the earlier the hearing loss was detected and treated—both medically and non-medically—the less would be the consequent effect upon the child's speech, language, and educational development. Assuming that the hearing loss was detected at an early age, we would now like to consider one vital aspect in the habilitation of such a child: hearing aid selection and usage.

No decision can be made regarding use of a hearing aid until the medical aspects of the hearing loss have been thoroughly explored. Once this step has been taken and it has been found that the child's loss is not medically reversible, the following decisions regarding the use of a hearing aid must be made: (1) Is the child a hearing aid candidate? (2) If he is, at what age should the aid be introduced? (3) What type of hearing aid should be used. (4) Which acoustical features must be incorporated. (5) Finally, what are the needs and extent of hearing aid orientation and training procedures for the child and his parents. (Specific training techniques, such as auditory training, lip reading, speech and language therapy, are beyond the scope of this paper and will not be discussed.)

## Is The Child A Hearing Aid Candidate?

In deciding on hearing aid candidacy the problem is not to determine whether the child can get along without a hearing aid, but whether he can get along better with one. This is the focal point of the evaluation and diagnostic therapy. The usual criterion for hearing aid candidacy has been a hearing loss of 30 dB or more in the better ear. This criterion, however, was developed and used for adults before the advent of the modern ear-level hearing aid. It no longer holds for adults and even less so for children. The criteria for children are more flexible and depend to a large extent upon the probable educational effects of the hearing loss. For example, a child whose hearing loss is much greater for the higher frequencies than for the lower ones may have less than a 30 db average loss, but he will nevertheless usually demonstrate a speech, language, and educational deficit which

a hearing aid may be of great assistance in helping to alleviate.

Most children with severe or profound hearing losses can use and derive some benefit from a proper hearing aid. It is perhaps not fully appreciated that very few—less than 10 per cent—"deaf" children have no residual hearing. While a hearing aid for these very profoundly hearing-impaired children will not enable them to understand speech solely by the auditory channel, it can enable them to discern the rhythm of speech, its phrasing, stress and intonational patterns. A hearing aid can provide sufficient sound to alert the child to look at a speaker's lips or to warn him of impending danger (i.e. a horn or a siren). Even a small remnant of hearing, when added to lipreading, enables the hearing-impaired child to understand speech better than when he uses only his vision. Furthermore, a hearing aid can help these children monitor their own voice to a certain extent, and thus improve the clarity of their speech. Given realistic expectations and goals, there are very few children with severe or profound hearing losses who cannot derive some significant benefit from a hearing aid in some important situations.

## Earliest Age For Hearing Aid Usage

The age at which we recommend a hearing aid has been steadily lowered as we learn more about language development and the effects of auditory sensory deprivation. At the present time, there appears to be a general consensus<sup>1</sup> that it is best to fit an aid on a child as early as possible. "As early as possible," in our framework, means as soon as we have a high degree of assurance that a hearing loss is indeed present. It is not uncommon to fit a one-year old child with a hearing aid; in some countries and in some clinics in this country, it is fairly common to fit six to nine month old children

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with hearing aids. It must be pointed out that the assurance we seek regarding the presence of a hearing loss is not synonymous with obtaining an audiogram. The presence or absence of a severe to profound hearing loss can usually be made on the basis of history, behavior, and reactions to controlled sound stimuli. Actual audiograms, on the other hand, cannot be obtained much before the child is three years old. If recommendations regarding the use of a hearing aid were to wait upon the precise measurement of auditory thresholds, then several of the most important years in language development would have been lost. The normal child's greatest progress in language development occurs between the ages of one and three years. By providing the hearing-impaired child with amplification during this period, we take advantage of the maturational stage most conducive to language development. As a general rule, the later the child is provided with amplification, the less he will ultimately be able to use his residual hearing for learning speech and language. Since hearing aids are recommended for children prior to obtaining definitive audiometric information, the control over the acoustical features and the follow-up procedures discussed below are particularly important considerations.

### **What Type Of Aid**

The type of aid we recommend for a child is primarily determined by the type and degree of hearing loss manifested by the child. For those very young children for whom detailed audiometric information has not yet been obtained, the hearing aid recommended is one which has sufficient flexibility—in terms of acoustic characteristics—so that the proper modifications can later be made as more information regarding the child's loss is accumulated. For these children, a single body-borne aid with a split cord (technically, a "Y" cord) and two receivers, one for each ear, is usually recommended. This type of aid usually provides, at least for children, a more desirable acoustic signal and permits better control over the acoustic characteristics than does a smaller ear-level hearing aid. Also, the body-borne aid is usually sturdier than the ear-level aid—which must be considered when dealing with children. The "Y" cord ensures amplified sound in both ears until the time specific measurements and recommendations can be made, thus preventing an erroneous monaural fitting.

For the older child with a known bilateral mild or moderate loss, the ear-level hearing aid is the one of choice for several reasons. Being at ear level, this type of aid is more favorably located to pick up speech than the body-borne aids; the problem

of clothing rubbing against the microphone and producing noise, which occurs in body-borne aids, is eliminated; no articles of clothing cover the microphone and thereby reduce the reception of higher frequencies; and, finally, this type of aid can easily be used in a binaural fashion—which is not true for the body-borne aids. However, because of the generally better fidelity and flexibility of body-borne hearing aids, it is advisable to wait until the child has developed some basic receptive language patterns before recommending an ear-level hearing aid.

Binaural hearing aids (i.e. a separate and complete hearing aid for each ear) are of great value providing the child has a mild-to-moderate, fairly symmetrical, bilateral hearing loss. With a binaural fitting, the child is better able to locate the source of sounds—which has safety as well as communicative implications—and can better understand speech in the presence of noise than is possible with a monaural hearing aid.

Some few children are fitted with a bone-conduction type of hearing aid. In this type of aid, the amplifier drives a bone-conduction oscillator which is placed on the mastoid process. The sound stimuli then by-pass the middle ear and directly stimulate the inner ear. However, the air-conduction route is the preferred one for sound transmission to the inner ear, and only those children with bilateral auditory atresias or chronic draining ears are fitted with bone-conduction hearing aids.

### **Acoustical Features**

As with the type of aid, the acoustical features to be incorporated depend primarily upon the type and degree of hearing loss manifested by the child. When this has not yet been determined the usual recommendation is for a hearing aid that amplifies a wide range of frequencies, has little internal distortion, and permits limiting the maximum sound pressure level delivered to the ear. In other words, the attempt is made to expose the child to the best possible acoustic signal, and to do it in a manner which does not overexpose him to loud sounds. The hearing aid's flexibility permits adjustments of the acoustical features as more information regarding the child's loss is obtained.

Most "deaf" children have some residual hearing, and most often this remaining hearing is concentrated in the lower frequencies. Most hearing aids do not amplify these lower frequencies well, or at all. For these children to receive any benefit from a hearing aid, it is necessary to amplify the frequencies they are capable of hearing. Therefore, particular attention is paid to the lower frequency



range being amplified by the hearing aid when the patient is a young severely hearing-impaired child.

The requirements for the older child with a mild-to-moderate hearing loss are very different. This child does not need particular emphasis in the lower frequencies; more often than not, the lower frequency range of the hearing aid must be moved upward and the higher frequencies emphasized. The frequency range amplified by the aid usually does not need to be as wide as is desirable for the younger child (though, certainly, other things being equal, the wider the better).

It is important that any child using a hearing aid does not need to turn the volume control up to maximum under normal use conditions. First, it is desirable that the child have sufficient reserve so that he can increase the volume when necessary. Second, much more internal distortion (which may seriously interfere with speech understanding) occurs when a hearing aid is used at maximum volume and output. In addition, the maximum sound pressure level output should always be less than the level which can be tolerated by the child; otherwise the chances of his successfully adjusting to the aid are limited.

### **Hearing Aid Orientation And Training**

In a recent study<sup>2</sup> of 120 children for whom hearing aids were recommended and obtained, it was found that only 20 to 30 per cent of the children were obtaining maximum benefit from their aids. This was attributed to the lack of adequate hearing aid orientation and follow-up of the child and parents. It is not possible, in other words, simply to recommend a hearing aid and trust that the problem has been solved. It is imperative that follow-up appointments be scheduled for all children who use hearing aids. The parent and child must be taught how to operate the hearing aid and take care of it; they must be made aware of problems in adjusting to hearing aid amplification; and, finally, their expectations regarding the benefits of hearing aid amplification must be realistic. A hearing aid may be in perfect operating condition, but if the earmold does not fit properly, or if the parents do not know how or when to insert

a battery, then the hearing aid can be of no value to the child. Improper hearing aid usage, for any reason, may actually be worse than using no hearing aid at all. Parents may attribute lack of expected progress to something other than inadequate amplification and they may discard the hearing aid or refuse to try others, thinking they are of no benefit to the child. The great possibilities of early hearing aid amplification for the speech, language, and educational development of the hearing-impaired child cannot be realized unless strict control is exercised over the use of the hearing aid.

By virtue of training and experience, the personnel in a speech and hearing clinic are uniquely competent to select and control the usage of hearing aids for the young child. These functions are an integral part of the speech and language therapy program given to these children in a speech and hearing clinic. It is recommended that physicians refer young children with known or suspected hearing losses to speech and hearing clinics for consultation and/or care. From both an educational and a medical point of view, early diagnosis and treatment of the hearing-impaired child increase the probabilities of an eventual successful adjustment to his handicap.

### **Summary**

The use of hearing aids by young hearing-impaired children, as one aspect in their habilitation, has been considered in this paper. The necessity for early, adequate, and supervised use of hearing aid amplification was discussed. The cooperation of all professionals involved with the hearing-impaired child is necessary to ensure the development of the maximum potential in these children.

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# The Hospitalized Child

Harris C. Faigel, M.D.

■ A child in the hospital is like Linus without his blanket.<sup>1</sup> He is banished from the security of home, imprisoned by the bars of his high-sided bed and fed institutional mush. His parents and his clothes are taken away and he is surrounded by strangers in frightening white. He is hardly ever shown the toilet or told how to get food or drink, and he is subjected to such a poking, prodding, and stabbing that it is no surprise that he may think he is being punished for being ill.

The normal child goes through recurring cycles of dependence and independence from birth through adolescence.<sup>2</sup> Two-year-olds are forever under mother's feet, and five- and eight-year-olds seem to measure distances by the length of their mothers' apron strings. At other ages these same children seem perfectly content without their mothers for hours and days on end.

The child who is separated from his family during a normal period of increased dependence is likely to be upset by his experience, all of his behavior may deteriorate, and he may become self-centered, demanding, and infantile. It is often much easier to forestall this kind of problem than it is to treat it.

## Emotional Problems Of Hospitalization

Hospitalism was recognized over forty years ago in an age of prolonged hospitalizations. Children who suffered it became slow and dull, were neither spontaneous nor outgoing in their behavior, and had learning problems. Modern hospitalitis seems different because the hospital stay is so much shorter, and the child rarely has time to become totally withdrawn before he is sent home.

Before his first birthday, a child needs intellectual stimulation and good maternal care if he is to mature normally. He must be played with, talked to, and given a chance to learn social behavior.

Between one and three a child develops a deep attachment to one mother figure. Unexplained separations from her tend to arouse anxiety, dependency, depression, withdrawal, and regression.

From four to six most children are in the oedipal phase of development, and banishment to the hos-

pital can take on the appearance of losing the oedipal struggle, thereby arousing feelings of unworthiness. Surgery during these years, especially genital surgery, may appear to the child to be an attempt at castration.

After six, separation from home makes infantile behavior patterns worse and regression more severe. All children regress during an illness to a very dependent state because illness removes the need for self-responsibility and returns the child to an infantile relationship with his caretakers.<sup>3</sup> The child who is emotionally well found can bear these episodes and can return to normal behavior when the illness is over. The child who is insecure and immature may not. This is especially true if his parents become insecure and consider him more vulnerable to recurrences of the disease which precipitated the original separation.

Adolescents are aware of the general good health of their peers, and they resent and deny their illnesses. Hospitalization can be a very trying time for them if they do not feel ill.

## Preparing The Child For The Hospital

The child who knows what to expect in the hospital accepts the experience better than the one who is surprised by it. Every child over the age of two can be told something and can be helped to traverse the difficulties of separation with a minimum of trauma. Many children are given the chance to visit a hospital in a nursery school group and become familiar with the place before they ever have to spend any time there.

Often, in trying to reassure a child, adults unconsciously stress the negative aspects of the situation and worry the child unwittingly. How much nicer it is for a child to learn about the nice things that can happen in a hospital than to be told that "it won't hurt." The anticipation of ice cream following a tonsillectomy is much better for a child than fear of the pain of the sore throat which accompanies the surgery.

There are many stories which can be read to young children about hospitalization, and many

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hospitals have prepared coloring books which can be used to familiarize the child with doctors, nurses, and hospitals.

### **In The Hospital**

Once inside the doors of the institution there are many things which can be done to make hospitalization less traumatic for the child. A familiar toy or blanket from home can often take the edge off fear, just as the presence of parents can. In most hospitals ward rounds are completed by 10:00 a.m. and there seems little reason, save administrative sclerosis, for keeping parents from their children once these chores are done. Young children thrive in groups and wilt in solitude. Private rooms only salve parental consciences; the real need for a private room in a children's ward is rare.

Parents are as capable of administering rub-downs and medicines, and of feeding and cleaning their children in the hospital as they are at home. When procedures are necessary, the presence of the parents can comfort the child and make the test easier to perform. However, when a parent's presence is detrimental to the child or himself, a parent rarely refuses to leave for the benefit of the child.

Naps go on in the hospital as they do at home. Open visiting hours until bedtime do not crowd a ward with families because most parents have other duties as well.

In hospitals where pastel uniforms for the staff have been used, physicians have discovered that their young patients adjust to the hospital routine more quickly and suffer fewer after effects than when the staff wears white.<sup>4</sup> Traditional whites just are not necessary, and pleasant colors are much more comforting to young children who have suddenly been thrust into a hospital bed.

Living-in is a great help to the child between one and five. During these years of great dependency upon and attachment to mother, a mother's presence in the hospital may completely dispel all of the child's anxieties.

Children confined to a bed usually use it as a trampoline and "bedrest" for a four year old may entail more physical activity than a quiet afternoon doing puzzles or finger-paintings in a playroom. Children love wheelchairs and wheeled carts and being able to sit in the hallway and see what is going on around them. They thrive on communal dining, and they eat better when they sit at the same table and watch other children eat.

When a child is ill, he limits his own activity. As he recovers he should be allowed as much activity as possible with very few exceptions.

Whenever possible, tests and procedures should be grouped together. There is no reason why a

child who has had a hemogram on Monday, a blood glucose on Tuesday, and serum electrolyte determinations on Wednesday could not have them drawn simultaneously with forethought. And how much easier for the child!

### **The Playroom**

It is almost negligence not to have a playroom in a well-organized children's ward nowadays. However, too often this is simply an area set aside for ambulatory patients to be away from their beds and cubicles. It is supervised, if at all, by nurses and aides whose minds are concerned with other duties.

The ideal hospital playroom serves three functions. It offers the child occupational play therapy to help minimize hospitalitis. It offers the disturbed child a highly structured environment in which his relationships with his parents, his peers, and adults can be studied. And in a psychiatric center, it offers the disturbed an adjunct to psychotherapy.

The well-ordered playroom is staffed with people who are trained in elementary education and in psychology. Their background in education helps them choose the right play for each child, and their knowledge of psychology is a valuable source of information in judging the relationships between a child and his family. Nurses are not necessary since any child who needs medication can have it brought to him or he can be returned to his ward for it.

The play-therapist should attend the same children each day so that she can function as a mother-substitute throughout the hospitalization. It is foolish to send a child to a playroom and have him see his newly acquired "mother" stolen by a rival. The family principle of a group of children under the care of one person, no matter whether she is a teacher, a nurse, a volunteer, or a play-lady is the most important factor in structuring the environment of the playroom for the benefit of the child.

### **Surgery**

Most of a child's fears of surgery are not caused by thoughts of anesthesia before or pain after the procedure. Parents of children who are about to undergo surgery are apprehensive and they betray their anxieties to their children who in turn become upset, not by the prospect of surgery, but by their parents.

The use of nitrous oxide for induction and halothane for anesthesia, combined with appropriate premedication can make surgery almost pleasant. Space-helmets and rubber toys rigged with anesthesia tubes for inductions make the introduc-

tion to the operating room with its bright lights, strange instruments and masked strangers more benign.

Children are remarkably tolerant of pain post-operatively, and they require very little analgesia. It is almost as if they were not expecting pain and therefore do not experience it.

### **The Physician And The Child**

"Little pitchers have big ears," and even larger imaginations. Children should be told the truth simply and straight-forwardly because they have an inborn radar which tells them when adults are lying. Half-heard and half-understood mutterings of hurried physicians or nurses on ward rounds can precipitate a severe reaction to hospitalization.

If there is something to be said which the child should not hear, the discussion should be held well out of earshot. The doorway of the room is not far enough away for the acute hearing of the young child.

### **Aftercare**

The physician must remember that the child who has been hospitalized recently may go through a period of acute dependency once he is home. He will be forever under foot, always turning up to be certain that he has not been abandoned and that his mother is still there. The physician should warn the parents of the possibility of this happening when the child is sent home, and he should ask the parents about it again at the followup visit. Many parents will not volunteer the information that their child has suddenly become very infantile, and they will be unable to help the child get over it without the help of their physician.

The child should be encouraged to talk about his hospital stay. Reminiscing will help stress the positive aspects of hospitalization—the child recovered and went home—and will help the child verbalize his anxieties and get over them more quickly.

The physician must make it clear to the parents when the child is fully recovered. He should point out that the emotional problems are the result of the separation from home and not an after-effect of the illness. He must help them understand the child's problem and show them how to give the child attention and affection wisely. He must also help them understand when recovery is complete so that they will not consider the child permanently damaged by his affair with the hospital, or by his illness. Given all of these, the child will recover completely from his hospitalization as well as from his illness.

### **Summary**

A child's stay in a hospital can be as damaging to his emotional development as dry air to a fish's gills. With forethought, most of the problems can be prevented or reduced in severity. Given awareness and understanding by the physician and the parents, the difficulties that do arise can be managed successfully.

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There is a matter of policy and procedure in our profession which will have to be decided. In my view, we encourage good men inept at original research to sacrifice their time and energy upon it when they should be perfecting themselves as bedside physicians.—*Sir John Parkinson*



# Chronic Suppurative Arthritis And Osteomyelitis With Unusual Late Sequelae Case Report

Murray A. Rosenberg, M.D., and Isaac Horowitz, M.D.

■ X-ray changes consequent to long standing chronic osteomyelitis with spread of infection to adjacent articulations and resultant joint changes has been previously described in the literature.<sup>1,2</sup> Butler<sup>1</sup> reported a 24 per cent incidence of suppurative arthritis complicating acute osteomyelitis. Capener<sup>3</sup> discussed the method of dissemination from foci of infection to adjacent joints in relationship to the vascular supply.

The following case is presented to demonstrate far advanced bone and joint changes that may result from chronic suppurative bone disease.

## Case Report

C.R.K., a 70 year old white male, sustained a battle wound of his left foot during World War I. Painful swelling developed which was thought to be due to "rheumatism," and he was treated for several years accordingly. In 1924, an x-ray examination of the foot reported a metallic foreign body on the plantar surface adjacent to the articulation of the os calcis and cuboid bones. The foreign body was removed surgically; however, the swelling and pain persisted, and in due course multiple draining skin sinuses developed over foot and lower leg. In 1935 repeat x-ray examination reported showing bony fusion of the tarsal joints with periosteal reaction of adjacent bones of the foot and ankle. Episodic drainage continued, and in 1955 the patient was admitted to West Haven Veterans' Hospital.

The physical examination at that time revealed the left foot to be rigid in neutral position at 90 degrees dorsi-flexion with absent ankle and sub-talar motion. Restricted movement was present at the first and second metatarsal phalangeal articulations. The lower leg was noted to be considerably edematous and scarred and the skin over the area of the foot was excoriated, indurated, and discolored and there was multiple draining sinuses present. The girth at the ankle joint was at least twice that of the opposite limb.

## Laboratory Data

Laboratory data included Negative serologic test for syphilis on two determinations. The Erythrocyte Sedimentation Rate was 28 mm. per hour. Blood counts and urinalyses were normal. Cultures of the draining sinuses revealed *Staphylococcus aureus* sensitive to chloromycetin, penicillin and erythromycin.

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Repeat chest x-ray examination revealed generalized pulmonary emphysema, but no evidence of active pulmonary disease.

The patient was treated with the appropriate antibiotics and bedrest. Drainage subsequently subsided and has been absent for the past three years.

## Roentgenologic Findings

The films of the left foot and ankle (figs. 1-4) demonstrate complete bony ankylosis of most of the articulations of the foot and ankle. Normal bone architecture and anatomic landmarks are lost. The interphalangeal articulations of the great toe and



FIGURE I

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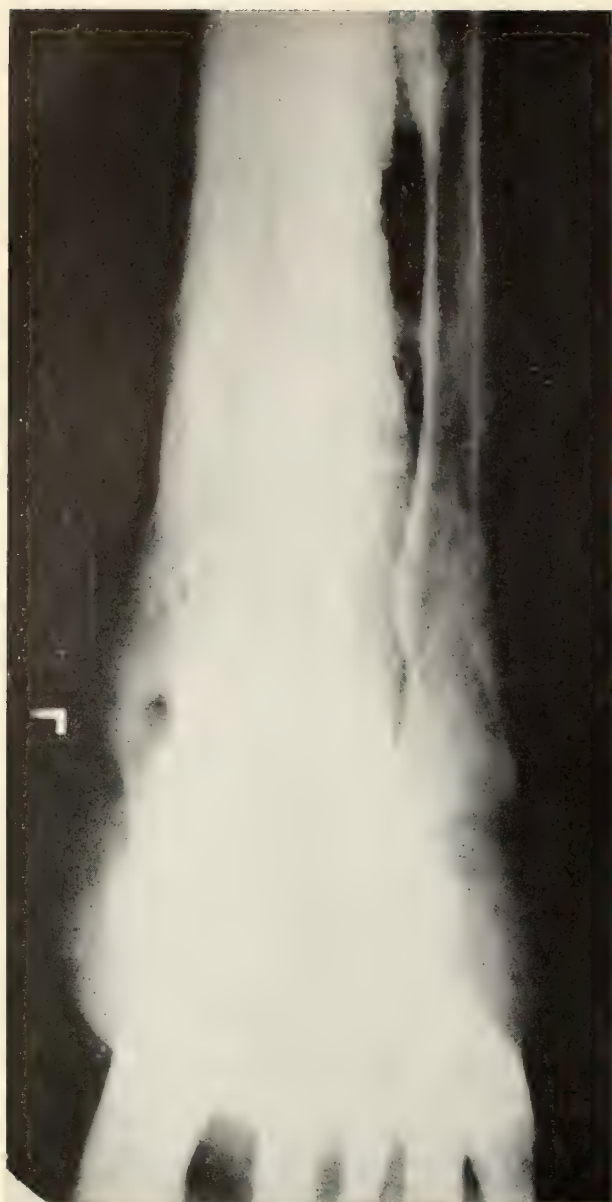


FIGURE II

the distal interphalangeal articulations of the remaining toes appear to be spared. Bridging and extensive periosteal thickening is present. On the lateral film of the foot, note that coarsened trabeculae have developed, crossing previous joint spaces. These appear to have been laid down according to the maximum weight bearing lines of stress. The new bone development behaves as if the tibia, ankle and foot were a single bone.

#### Discussion

The x-ray appearance of chronic osteomyelitis and pyogenic arthritis are quite typical and usually offer no challenge. However, on occasion, other entities may cause difficulty in establishing a diagnosis.

#### 1. FUNGUS INFECTIONS

A. *Mycetoma Pedis* (Madura foot) is an endemic lesion seen in tropical and subtropical areas.<sup>4</sup> The bone changes are marked and include extensive lamellar periosteal new bone formation with perpendicular spicules radiating from the cortex. The spongy portion of the bone shows increased

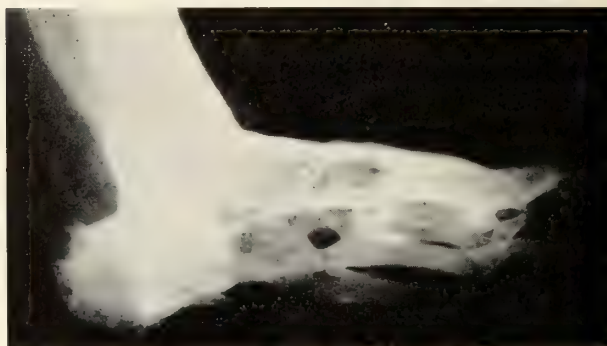


FIGURE III



FIGURE IV



sclerosis and loss of normal trabecular pattern. The changes may be so severe in structure, particularly in the bones of the foot, that it is impossible to identify the original bone landmarks.<sup>5,6</sup> The skin sinuses are filled with necrotic tissue and exudates containing yellow, red or black fungus granules.

B. Other fungus infections including *Cryptococcosis* may show x-ray changes similar to pyogenic arthritis. However, with *Cryptococcosis* the osseous lesions (bone destruction) are usually limited in extent and periosteal reaction is not marked.<sup>7</sup> Gram stain and cultures are usually sufficient to differentiate the causative agent from coccal organisms.

II. *Osteoarticular tuberculosis* and *tuberculous osteomyelitis* are usually manifest by destructive bone disease with little or absent sclerosis or new bone formation. Joint narrowing is a late manifestation.

III. *Syphilitic osteomyelitis* may result in extensive periosteal reaction with sclerosis and deposition of new bone. However, fusion and ankylosis is uncommon.

IV. In younger patients, *Ewing's sarcoma* and *osteoblastic osteogenic sarcoma* may present a similar x-ray appearance. However, joint involvement is uncommon and ankylosis is not seen with malignancy of bone.

## Conclusions

An unusually severe case of ankylosis of the foot and ankle following chronic suppurative osteomyelitis and arthritis of at least thirty years duration is presented.

In addition to extensive periosteal new bone formation, coarsened trabeculae were laid down corresponding to maximum lines of stress and unrelated to previous anatomic landmarks.

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## Physician-Patient Rapport

When you start to talk to a patient you should realize that your attitude toward him and your reaction to his complaints will create more of an impression than your technical skill or medical knowledge. The ability to be interested, unhurried, careful, tactful and considerate, rather than amused, supercilious, distracted, bored or inconsiderate of his sensibilities might well be called the essence of the art of medicine.—H. U. Hopkins, M.D., Ed., *Leopold's Principles and Methods of Physical Diagnosis*. Third Edition. 1965, p. 2.

# Diagnostic Problems Of Regional Enteritis

William A. Hoffman, M.D., and Murray A. Rosenberg, M.D.

## Introduction

■ Most patients with regional enteritis present with abdominal pain, fever, diarrhea, and weight loss. On occasion, we are faced with an unusual clinical picture or with non-specific x-ray findings or both. In some instances, we must resort to surgery to confirm the diagnosis.

Those patients that vary from the typical course of this illness present with the following problems.

### I. Atypical clinical findings.

A) The gastro-intestinal hemorrhage.

B) The findings resembling ulcerative colitis.

C) The acute abdomen.

### II. Atypical x-ray findings.

### III. Atypical clinical and x-ray findings.

#### I. A) Gastro-Intestinal Hemorrhage

Gastro-intestinal bleeding is not considered a cardinal sign of regional enteritis. Van Patter in reviewing 600 cases of regional enteritis described an incidence of gastro-intestinal bleeding of 16 per cent; 10 per cent of these patients had some streaks of red blood in their stools; 2.5 per cent of these patients passed profuse red blood in their stools; and 3.5 per cent of these patients had tarry stools.<sup>15</sup>

Daffner and Brown noted gastro-intestinal bleeding in 34 of 100 patients, but only four of their patients had frank melena and one patient had a duodenal ulcer.<sup>3</sup> Van Patter commented that 4 per cent of his cases had an associated duodenal ulcer, a percentage no higher than that found in the general population.

The following cases illustrate the problem of melena in the patient with ileitis. In Case No. 1 the patient had a peptic ulcer history and the melena had been attributed to this cause. Although a nasogastric tube was not used in attempting to localize the bleeding source, we feel that with the demonstration on x-ray of duodenal ulcer, this was the most likely cause of the bleeding.

Patient No. 2, in contrast, had ileitis with no other demonstrable source of gastro-intestinal pathology. At the time of her acute bleeding episode, no evidence of upper gastro-intestinal bleeding was noted. This case demonstrates melena due probably to regional enteritis.<sup>4, 6</sup>

#### Case 1—W.L., No. 4264-61

A 27 year old white married male was admitted to the hospital in May, 1961, because of weakness, pallor, and a hematocrit of 21 per cent. He had an episode of melena four

hours prior to admission, unaccompanied by abdominal pain, nausea, or vomiting. In 1951 the patient was told that he had "ulcerative colitis." In 1960 he was hospitalized following three days of melena and weakness. The hematocrit was 17 per cent. Barium enema was normal and the upper gastro-intestinal series demonstrated a duodenal ulcer which was confirmed on repeat studies one year later. Small bowel films revealed diseased loops of ileum. The pathological findings were confirmed at surgery, at which time a duodenal ulcer was palpated.

#### Case 2—S.Z., No. 2914-61

The patient was a 44 year old married white female, with a 17 year history of recurrent abdominal pain, cramps, diarrhea, and weight loss. Regional enteritis was diagnosed many years before based on x-rays of the small bowel. She was admitted in 1961 with a one day history of tarry stools. There was no hematemesis. The patient had been taking propantheline bromide on occasion but no other medication. There were no peptic ulcer symptoms. On admission, the patient had a pulse of 104 and a blood pressure of 130/80. The general examination was unremarkable except for pallor and hyperactive bowel sounds. The hematocrit was 23 per cent. Naso-gastric intubation produced no evidence of blood in the stomach. A small bowel series shortly after admission revealed changes of regional enteritis. (Fig. 1). There was no evidence of ulceration of the stomach or duodenum. The findings by x-ray are very typical of the non-stenotic phase of ileitis.

#### I. B) Mimicking Ulcerative Colitis

A more difficult problem rests in distinguishing granulomatous colitis from ulcerative colitis. Recent work has stressed the distinctive features of these illnesses; much of this work however is retrospective. The sigmoidoscopic changes in regional enteritis are well recognized.<sup>2, 9</sup> In Case No. 3, the rectal biopsy was non-specific.

Lockhart-Mummery reported 25 cases of granulomatous colitis and noted localization to the rectum in six.<sup>9</sup> Rectal involvement may be seen with or without small bowel disease. Typical granulomatous colitis (regional enteritis of the large bowel) with rectal involvement may reveal small or large ulcerations with intervening normal mucosa. In

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FIGURE I

Small bowel series. Note the marked "cobble stone" appearance of the ileum just distal to a short segment of narrowed bowel. The longitudinal streaks of barium and the "cobble stone" appearance indicate that ulcerations have occurred leaving intervening islands of inflammatory mucosal thickening.

ulcerative colitis, the entire mucosa is friable, congested, and granular; biopsy in well defined cases shows crypt abscesses.

Carnes and Stecher point out that the majority of rectal biopsies in cases of enteritis do not show typical "tuberculoid" reaction.<sup>1</sup> In the individual patient with an ulcerated and bleeding rectal mucosa and a nonspecific biopsy, the diagnosis of regional enteritis or granulomatous colitis becomes difficult to establish. The subsequent clinical course and x-ray changes of the small bowel or right colon establish the diagnosis of granulomatous disease.

In a patient with x-ray evidence of regional enteritis the association of large bowel pathology indicates a similar process in the colon. Patient No. 3 was thought to have ulcerative colitis and it

is now evident that he has regional enteritis. Ulcerative colitis and regional enteritis may coexist in the individual patient. In such a case the rectal biopsy would have to demonstrate the characteristic pathologic changes of ulcerative colitis, i.e., crypt abscesses.<sup>8, 14</sup>

### Case 3—T.K., No. 6195-62

A 26 year old white male was first admitted to the hospital in March 1960 following burning pain in the anus and rectal bleeding. He complained of frequent stools and weight loss for approximately five months. Physical examination revealed an anal ulcer. Sigmoidoscopy to 24 cm. was normal. The patient had a hemorrhoidectomy and excision of a fissure-in-ano. In October 1960 he was hospitalized in another institution where a diagnosis of ulcerative colitis was made. He was admitted to our hospital in January 1961 with rectal bleeding and bloody diarrhea. Physical examination was normal. Sigmoidoscopy revealed spasm and a friable rectal mucosa. The barium enema was negative. A hematocrit was 43 per cent. He was readmitted in November 1961 with a similar history of rectal bleeding and was treated with adrenal cortical steroids. Sigmoidoscopy again revealed spasm and a friable mucosa. A rectal biopsy showed chronic inflammatory changes without evidence of crypt abscesses. In 1962 he was again admitted because of diarrhea, rectal bleeding and continued weight loss in spite of steroid therapy. Sigmoidoscopy and rectal biopsy showed similar findings to those seen on



FIGURE II

Barium enema. Note the rigid ileo-cecal valve and narrowed terminal ileum as it enters the valve. Note also the normal mucosal pattern of the large bowel distal to the cecum. (Upper arrow: Distended duodenal loop). Involvement of the duodenum is not infrequently seen.<sup>11</sup>

the previous admission. His hematocrit was 42 per cent. X-ray studies showed changes in the terminal ileum and duodenal loop consistent with enteritis. His dosage of steroids was increased and at the present time he is asymptomatic. (Fig. 2).

### I. C) Acute Abdomen

The following cases illustrate that regional enteritis may present as a surgical abdomen. Case No. 4 was thought to have an acute appendicitis. Case No. 5 was diagnosed as a small bowel obstruction. The diagnosis of regional enteritis in a patient who presents a clinical picture of acute appendicitis is usually made at surgery. Abdominal pain is seen in approximately 80 per cent of the patients with enteritis. Since the ileum is the most frequent location of the disease, abdominal pain referred to the umbilicus or localized to the right lower quadrant is not unusual. In a large series of patients with ileitis about 25 per cent of the patients had a history of appendectomy. In the individual patient, coincidental appendicitis may occur although the combination is rare. At the Mayo Clinic 30 per cent of their 600 cases had operations performed because of suspected acute appendicitis.<sup>15</sup>

Severe narrowing of the bowel lumen from acute inflammation, or more likely fibrosis, may lead to a clinical picture of intestinal obstruction. In our experience, complete mechanical small bowel obstruction complicating ileitis has been rare. We have recently seen an acute obstruction occurring one day after the sudden cessation of prednisone.

#### Case 4—L.K., No. 764-63

A 36 year old white female was admitted with a history of severe right lower quadrant pain of several hours duration. She had anorexia and vomiting for three days prior to admission. Her general health had been good. Physical examination revealed right lower quadrant tenderness and associated guarding. Pelvic examination revealed exquisite tenderness in the right adnexa. A white blood count was 12,400. A urinalysis was negative. Her temperature was 100°F. A laparotomy was done with a pre-operative diagnosis of acute appendicitis. At surgery the entire distal ileum appeared boggy and nodular. The gross clinical impression was regional enteritis. Histological sections indicated involvement of the appendix. Bowel resection was not done but the appendix was removed. A small bowel series six months later confirmed the diagnosis of regional enteritis. To date the patient has been asymptomatic and has not required medication.

#### Case 5—C.D., No. 5885-60

A 44 year old white male was admitted in August 1960 with a six month history of abdominal pain. He had had an appendectomy in 1945. Prior to admission the patient experienced pain in the epigastrium which was not related to food, antacids, or bowel movements. There was no history of bleeding or diarrhea. He appeared chronically ill and abdominal examination revealed a tender mass in the right lower quadrant. Stools for occult blood were negative. A white blood count was 10,800. Clinical and roentgenographic find-



FIGURE III

Small bowel series. The bowel loops are markedly dilated with an area of abrupt narrowing seen in the terminal ileum. The smooth edges of the dilated bowel indicate a probable benign constriction.

ings suggested mechanical small bowel obstruction. (Fig. 3). A laparotomy was done and a very thickened distal ileum with a markedly narrowed lumen was found. There were two skip areas in the proximal ileum. An ileotransverse colostomy was performed. Pathological examination revealed regional ileitis.

## II. Atypical X-ray Findings

### A. NON-SPECIFIC SMALL BOWEL PATTERN CHANGES

X-ray changes in the malabsorptive syndrome are non specific. The mesenteric form of lymphosarcoma may manifest with generalized mucosal edema. Segmentation, fragmentation and dilatation of bowel loops may be seen in varying degrees in nontropical Sprue, pancreatic insufficiency and Whipple's Disease.<sup>12</sup> The non-stenotic phase of regional enteritis may show coarsened folds and altered bowel motility.<sup>10, 13</sup>

Case No. 6 illustrates the difficulty in diagnosis because of these non-specific x-ray finding. The patient had typical features of enteritis, i.e., diarrhea, colic, weight loss and fever. Laboratory evidence supported the diagnosis of a malabsorptive syndrome. The small bowel biopsy was normal, eliminating sprue, Whipple's Disease and other



diffuse, but non-specific changes. Surgery in such cases establishes a definite diagnosis and offers a clinical remission by removal of the diseased small bowel. Because of the high rate of recurrence after resection, surgery usually should be reserved for the complications of enteritis.

**Case 6—A.Z., No. 6825-62**

A 55 year old married white female presented with a weight loss of 30 lbs. She was in good health until one year prior to admission. Three weeks prior to admission she developed watery diarrhea, abdominal cramps, and fever. She was anorexic, complained of "gas," and experienced several episodes of vomiting. Her blood pressure was 100/70, pulse 120. The patient appeared thin, chronically ill, and older than her chronological age. Her tongue was red and beefy with atrophic edges. The abdomen was soft and without palpable masses. There was generalized tenderness and bowel sounds were active. Laboratory studies suggested a problem with intestinal absorption. A hematocrit was 35 per cent a serum carotene level was 40 micrograms per cent. A small bowel biopsy revealed mucosal edema, a non-specific finding. X-rays revealed generalized changes consistent with the diagnosis of malabsorptive syndrome. The patient suffered recurrent bouts of fever and diarrhea. Steroid therapy was initiated and she was discharged. Because of persistent symptoms, she was admitted to Yale-New Haven Hospital two months later where changes of regional enteritis were found at surgical exploration. An ileo transverse colostomy with resection of terminal and ascending colon was performed. Postoperatively the patient has done well and is now asymptomatic and gaining weight without medication. She is receiving parenteral Vitamin B<sub>12</sub> monthly.

**II. B) Changes Of The Cecum Resembling Malignancy**

It is well recognized that cancer of the cecum may be demonstrated by barium enema x-rays merely by contraction and irritability of the caput cecum without discernible tumor; in addition, inflammatory processes adjacent to the cecum, particularly on the medial aspect, may cause sufficient changes to mimic an intra-luminal tumor of the bowel.<sup>5,7</sup>

In patients No. 7 and 8 the x-ray studies were consistent with primary disease of the cecum. In Case No. 7 an intra-luminal polypoid filling defect was noted and carcinoma considered. At surgery the changes were found to be caused by the inflammatory mass of ileum intussuscepting into the cecum. In Case No. 8 the caput cecum was markedly contracted and foreshortened and an infiltrating carcinoma had to be excluded.

In these patients a thorough small bowel series would have revealed the presence of ileitis as the cause of cecal changes.

**Case 7—G.D., No. 2456-61**

A 52 year old married white male was admitted with a six months history of crampy right lower quadrant pain asso-

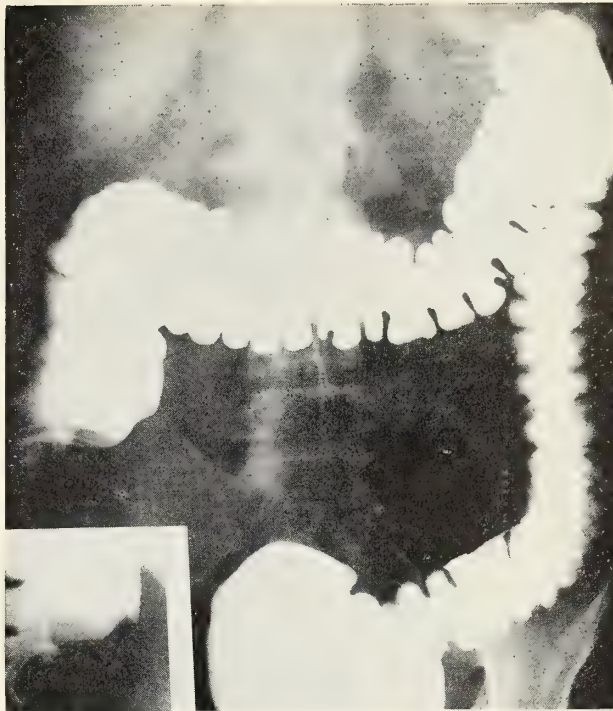


FIGURE IV

Barium enema examination and pressure spot film of the cecum show an intussuscepting intra-luminal mass appearing radiographically as a polypoid neoplasm.

ciated with diarrhea and weight loss. Physical examination revealed tenderness in the right lower quadrant where an orange size mass was palpated. Barium enema demonstrated a filling defect of the cecum. (Fig. 4).

At surgery a right hemicolectomy was performed. The terminal ileum was adherent to the cecum by an indurated mass. This was felt grossly to represent terminal ileitis and was confirmed by pathological examination. In addition, an intramural abscess of the cecum and a fistula existed between the ileum and caput cecum.

**Case 8—M.M., No. 7692-62**

The patient was a 67 year old white female admitted in 1962 with a six months history of episodic vomiting, diarrhea, and right sided abdominal pain lasting up to one week. She had three to four bowel movements a day associated with rectal bleeding. An appendectomy had been performed in 1944 and the patient remembered having a prolonged drainage from the wound. She also had episodic diarrhea following this operation. Physical examination was unremarkable. The hematocrit was 41 per cent. X-ray studies could not exclude carcinoma of the cecum possibly involving the ileo-cecal valve. At laparotomy extensive adhesions about the distal ten feet of small bowel were encountered. There was considerable thickening and induration and sensation of a mass behind the cecum. A small bowel resection and ileo-transverse colostomy was performed. Pathological examination revealed regional ileitis with ulceration and sinus tract formation and involvement of the adjacent lymph nodes. The patient was readmitted to the hospital in December 1963 with an acute myocardial infarction. At that time there was no further evidence of gastro-intestinal difficulties.



FIGURE V

Small bowel series shows extreme dilation of the proximal small bowel with intervening areas of stenosis and marked mucosal edema.

### III. Atypical Clinical And X-ray Findings

Case No. 9 illustrates the problem of a patient with known ileitis who is proven to have an unrelated abdominal disease. This patient had had several small bowel resections and short circuiting procedures for enteritis in the past. At first it was presumed that her abdominal mass represented chronically inflamed bowel loops probably complicated by abscess formation. At surgery the finding of an ovarian tumor was fortuitous.

#### Case 9—E.G., No. 6179-63

A 39 year old unmarried white female was admitted in July 1962 because of nausea, vomiting, abdominal pain and diarrhea of several months duration. In 1941 the patient had an ilco-transverse colostomy for regional enteritis. She remained in good health until 1956 at which time she again experienced diarrhea and weight loss. A small bowel resection was performed for intestinal obstruction. One year later an abdominal sinus tract developed which was treated by incision and drainage. She did well until 1962. Her abdominal findings were unremarkable except for multiple abdominal scars. Sigmoidoscopy was normal. Pelvic examination revealed a very large, firm mass. The patient was started on steroids with some symptomatic improvement. She was later admitted to another hospital where a large

cystadenoma of the left ovary was removed. She has been asymptomatic since this time. (Fig. 5).

### Summary

1. Selected cases of regional enteritis are presented to illustrate the difficulty in arriving at a correct diagnosis because of confusing and complicating clinical or x-ray patterns, or both.

2. In patients with gastrointestinal hemorrhage or those presenting with acute abdomen, the possibility of regional enteritis should always be considered.

3. Patients with ulcerative colitis, particularly in cases where rectal biopsy and x-ray findings are not typical, should be considered as having possible regional enteritis and/or granulomatous colitis.

4. Cecal involvement in regional enteritis can often simulate an infiltrating or polypoid neoplasm.

We would like to thank Drs. H. M. Spiro (New Haven), M. Elkin (Bronx, N.Y.) and R. R. Goldin (Bronx, N.Y.) for their critical review and suggestions.

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# Connecticut State Medical Society

## SCHOOL HEALTH

## NEWSLETTER

No. 1

November 1966

*This is the first of a series of three newsletters on school health subjects which has been authorized by the Council for publication in the Journal. Reprints of each issue will be made available to the State Commissioners of Health and Education for distribution to personnel within their respective Departments.*

This page is directed at all Connecticut physicians since all of you, like it or not, have a stake in education for health. If you don't believe it, read on and think.

This newsletter is for you. It will note, highlight, and review events, experiences, and publications pertinent to the health of school children.

Physicians do not realize that modern school health programs are far more than mere inspection of partly clothed bodies. A good school health program must include (1) proper public health and sanitation in the school plant; (2) health education; (3) the screening for physical defects; (4) proper physical education; (5) provision for a healthy emotional atmosphere; and (6) programs adapted for the handicapped child.

### Basic Facts

In 169 towns in Connecticut there are 881 public elementary schools and 230 secondary schools with a total enrollment of 574,798 pupils. These are your present and future patients.

There are 274 physicians officially designated as school medical advisors serving over 500,000 pupils. Many more of us participate indirectly through performing school health examinations and by advising parents and school personnel.

### Food For Thought

#### 1. Venereal disease

The State Department of Health statistics indicate a startling increase in the incidence of gonorrhea in Connecticut teenagers. In 1964, it reported 284 new cases. The 1965 report revealed 402 new cases. In 1965, there were 16 cases of primary and secondary syphilis in the 15-19 year age group.

#### 2. Growth

54 per cent of mature height is obtained by 3 years of age; another 32 per cent is added by 12 years of age.

#### 3. Development

50 per cent of the growth in the ability to learn (intelligence) is made by 4 years of age and 80 per cent is accomplished by 8 years of age.<sup>5</sup>

#### 4. Family Living

Nationally in 1964 there were 268,000 American infants born out of wedlock representing a rise of 24 per cent since 1960. In Connecticut, in 1965, teenage mothers accounted for roughly one-third (1002) of the State's total illegitimate live births.

## Research

### 1. *Disease and Defects*

In a composite adolescent population referred to 19 Clinics in California the following diagnoses were made in the percentage noted:<sup>4</sup>

|                        |             |                                   |             |
|------------------------|-------------|-----------------------------------|-------------|
| 1. Obesity             | 74 per cent | 7. Menstrual Disorders            | 21 per cent |
| 2. Acne                | 63 per cent | 8. Mental Retardation             | 21 per cent |
| 3. Allergy             | 42 per cent | 9. Growth and Metabolic Disorders | 21 per cent |
| 4. Seizures            | 31 per cent | 10. Normal Adolescent             | 16 per cent |
| 5. Orthopedic Problems | 31 per cent |                                   |             |
| 6. Infectious Disease  | 26 per cent |                                   |             |

Twenty different organic diseases accounted for 60-75 per cent of the above list. Emotional disorders were noted in 25-40 per cent of the patients in various clinics.

### 2. *Follow up of Clinical Problems*<sup>7</sup>

In a study of health defects referred by schools in New Haven, follow up by parents was related to family characteristics. Family understanding of the seriousness of a referred health problem leads to action in follow up. The acute problems are looked upon as being of more consequence than chronic problems. Social, cultural or economical variations in families apparently had little effect on action taken.

Factors that appeared to be positively related to effective follow up were: length of residence in town; literacy of parents; and the ownership of health insurance.

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If you've read this material, thought about it and like it or feel critical, let us know.

Advisory Committee on School Health  
Connecticut State Medical Society  
Joseph J. Bellizzi M.D., *Chairman*

*Prepared for publication by the CSMS Advisory Committee on School Health.*



# THE PRESIDENT'S PAGE

## The A.M.A. Takes Constructive Action

**I**N recent years, the press and other communication media have created the impression in the minds of the people that organized medicine is chiefly interested in financial matters. The fact that the A.M.A. has more than 100 working Committees and a vast number of Councils dealing with diverse aspects of medical affairs goes virtually unrecognized. Recent activities of the Association in the interest of the welfare of the public have dealt with the major problems of Medical Quackery on the one hand and Medical Education on the other.

Early in October, the Third National Congress on Medical Quackery was held in Chicago. Quackery, defined in a broad sense, refers to false pretensions of medicines, mechanical devices, or possession of skills to cure disease. Since the medical profession finds these practices intolerable, this subject provided a broad base for discussion and action. It also provided a forum for a review of many aspects of current drug surveillance. Charlatanism is a relative quality varying in degree, dependent on the level of knowledge at a given time and individual conscience. The use of "water from the depths of the sea containing sodium chloride" as a cure-all perhaps had more scientific justification during the early era of identification of the chemical elements than the use of uranium pads having as much radioactivity as the dials of a wrist-watch has for the "cure of arthritis" today. Combined with clever slogans and deceptive names subtly extolling special virtues for such products without reference to any bona fide ingredients, the suggestible public is induced to spend billions of dollars. It is not only the cost of these items purchased on the basis of false faith which is of concern. The waste of money is incomparable with the loss of health and indirect ill-effects which may occur from delay in seeking authentic and effective methods of treatment. Harm, and even irreversible damage, to health may result from methods employed by quacks. Industries concerned with the production and distribution of drugs and other accoutrements for the practice of medicine, medical researchers, representatives of the A.M.A. and the government are actively engaged in applying methods to ensure reliability of products and safety for their use by the public.

At the request of the A.M.A., a Citizens Commission on Graduate Medical Education was formed. Recently, the Committee has reported on its deliberations concerning: (1) present standards of education, (2) needs for the foreseeable future, and (3) mechanisms by which medical educational responsibilities may be met. Embodied in their specific recommendations, methods are proposed which take cognizance of today's complex requirements of a profession in which "a continuing infusion of knowledge makes continual change imperative." Much time and effort has been exerted in the endeavor to find ways which will ensure high quality medical care.

These important activities on the part of organized medicine, and many others which are frequently overlooked, are commendable and obviously in the interest of the public.

ORVAN W. HESS, M.D.

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**Warning:** Patients who experience dizziness, lightheadedness, or feelings of detachment on INDOCIN should be cautioned against operating motor vehicles, machinery, climbing ladders, etc. Use cautiously in patients with psychiatric disturbances, epilepsy, or parkinsonism.

**Precautions and Adverse Reactions:** Most commonly, headache, dizziness, lightheadedness, G.I. disturbances. The C.N.S. effects are often transient and frequently disappear with continued treatment or reduced dosage. The severity of these effects may occasionally require cessation of therapy. G.I. effects may be minimized by giving the drug with food or with antacids or immediately after meals. Ulceration of the stomach, duodenum, or small intestine has been reported and, in a few instances, severe bleeding with perforation and death. Gastrointestinal bleeding with no obvious ulcer formation has also been noted; INDOCIN should be discontinued if G.I. bleeding occurs. As a result of G.I. bleeding, some patients may manifest anemia, and for this reason periodic hemoglobin determinations are recommended. Rare reports of effects not definitely known to be attributable to INDOCIN include bleeding from the sigmoid colon (either from a diverticulum or without a known previous pathologic condition), perforation of preexisting sigmoid lesions (diverticulum, carcinoma), and hematuria. In other rare cases, a diagnosis of gastritis has been made while the drug was being given. One patient developed ulcerative colitis, and another, regional ileitis, while receiving INDOCIN; when the drug was given to patients with preexisting ulcerative colitis, there was an increase in abdominal pain. Infrequently observed side effects may include drowsiness, tinnitus, mental confusion, depression and other psychic disturbances, blurred vision, stomatitis, pruritus, edema, and hypersensitivity reactions. Slight BUN elevation, usually transient, has been seen in some patients, although the preponderance of evidence indicates that INDOCIN does not adversely affect renal function, even in patients with preexisting renal disease. Nevertheless, renal function should be checked periodically in patients on long-term therapy. Leukopenia has been seen in a few patients. Transient elevations in alkaline phosphatase, cephalin-cholesterol flocculation, and thymol turbidity tests have been observed in some patients and, rarely, elevations of SGOT values; the relationship of these changes to the drug, if any, has not been established. As with any new drug, patients should be followed carefully to detect unusual manifestations of drug sensitivity. Before prescribing or administering, read product circular with package or available on request.

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## CALL

### SEMI-ANNUAL MEETING OF THE HOUSE OF DELEGATES

**The 1966 Semi-Annual Meeting of the House of Delegates will be held at the Connecticut Light & Power Building, Berlin Turnpike, Berlin, commencing at 2:00 o'clock in the afternoon of Thursday, December 8.**

**Orvan W. Hess, President**

**Kenneth F. Brandon, Speaker of the House**

**Waldo E. Martin, Secretary**

## INTRODUCTION OF RESOLUTIONS

Article V, Section 12, Par. 3 of the Bylaws of the Society Provides that:

*All resolutions to be considered as regular business at any regular meeting of the House of Delegates must be in the hands of the Speaker not later than seventy-two hours before the opening of that meeting. All resolutions and recommendations published in the official agenda distributed to the members of the House prior to the meeting at which action is to be taken shall be considered as regular business. Resolutions presented later than seventy-two hours before the opening of a meeting will be referred for consideration as regular business by the House only when they are presented by the Council or accepted for consideration by majority vote of the delegates present. Any resolution which does not qualify in accordance with the aforesaid provisions for consideration as regular business may be accepted for action by a majority vote of the delegates present and, if so accepted, shall be referred at once by the Speaker to a reference committee. Any such reference committee shall consider resolutions referred to it and shall report, with recommendations to the House before adjournment of the meeting.*

## PROPOSED AMENDMENTS TO THE BYLAWS

**The following proposed amendments to the Bylaws were presented to the House of Delegates on April 26, 1966 and were tabled for consideration and action at the next regular meeting of the House of Delegates.**

**In accordance with the Bylaws, these amendments will be published in Connecticut Medicine, "on one or more occasions prior to the next meeting . . . at which meeting the amendments shall be taken off the table and acted upon by the House of Delegates."**

### INTRODUCED BY THE COUNCIL:

I. *To delete or change the name of certain committees, and make editorial corrections.*

(a) *To delete the "Conference Committee for the Improvement of Care of the Patient."*

Article X—Committees of the Council.

Section 3. Representatives and Advisors.

Amend *Paragraph 1. Outline to delete "Conference Committee . . . Patient". Amend Paragraph 9. Conference Committee . . . Patient to delete the entire paragraph, and renumber Paragraphs 10-16 to become Paragraphs 9-15.*

(b) *To change the name of the Advisory Committee on Medicare Plan, etc. to avoid confusion with P.L. 89-97 (Medicare for the Aged).*

Article X—Committees of the Council.

Section 3. Representatives and Advisors.

Amend *Paragraph 1. Outline to list this committee as: "Advisory Committee to the Office of Dependents Medical Care and Federal Employees Health Benefits Program".*

Amend *Paragraph 3 to read: "Advisory Committee to the Office of Dependents Medical Care and Federal Employees Health Benefits Program", and make editorial changes in the first paragraph of the descriptive text as follows:*

*"The Council shall elect annually an Advisory Committee to the Office of Dependents Medical Care and the Federal Employees Health Benefits Program and appoint the Chairman thereof." (The balance of the text remains the same).*

(c) *To include other medical schools within Connecticut in the "Committee on Cooperation with the Yale School of Medicine" and to stimulate initiative in the Committee.*



Article XI—Divisional Boards and Committees.

Section 3. Divisional Standing Committees.

Amend second listed committee name in (A) *Education and Hospitals Division* to read: "Committee on Cooperation with the Medical Schools of Connecticut".

Section 5. Duties of Standing Committees.

Amend Paragraph 2 to read: "Committee on Cooperation with the Medical Schools of Connecticut", and make editorial changes in the text to conform with the change in name and broadening of the scope of the Committee as follows:

"The Council annually shall nominate to the House of Delegates a Committee on Cooperation with the Medical Schools of Connecticut to consist of not less than three nor more than seven members and shall nominate the chairman thereof. The function of the committee shall be to study the educational programs of the medical schools, to provide information for members of the Society and for the faculties and governing bodies of the medical schools on matters related to this subject and, as occasion arises, to enlist the support of members of the Society in assisting the medical schools in its educational programs. The Committee should take initiative in developing such activities, as well as cooperating with the medical schools when requested."

(d) *To recognize the separation of the Sections on Ophthalmology and Otorhinolaryngology.*

Article XI—Divisional Boards and Committees.

Section 5. Divisional Standing Committees.

Amend Paragraph 20. *Committee on Eye Care* by deleting the words (starting at the end of line six) "Ear, Nose and Throat".

(e) *To completely delete reference to a "Liaison Committee with CMS, Inc."*

Article XI—Divisional Boards and Committees.

Section 5. Divisional Standing Committees.

Amend Paragraph 13. *Committee on Third Party Payments* by deleting the words (starting in line thirteen) "those of the Liaison Committee with CMS or".

(f) *To change the name of the "Committee on Emergency Medical Care", and list same.*

Article X—Committees of the Council

Section 3. Representatives and Advisors.

This Committee was reactivated in 1961, but has not been listed in the Bylaws. Further, the Council has already approved a change in name to: "Committee on Disaster Medical Care". It would seem logical to place this Committee under Section 3 of Article X (Council "Representatives and Advisors"), designate it as "advisory," and describe its composition and functions, as follows:

Amend Paragraph 1. *Outline* by adding: "Advisory Committee on Disaster Medical Care"

Amend Section 3. *Representatives and Advisors* by adding a new Paragraph 17, to read:

"Par. 17. Advisory Committee on Disaster Medical Care. The Council shall annually elect an Advisory Committee on Disaster Medical Care, to consist of not less than six members, and appoint the chairman thereof. The purposes of this committee shall be to study and keep informed on matters pertaining to the planning of programs designed to provide continuing medical care to the people of Connecticut under disaster conditions; to cooperate with other agencies in the State engaged in similar activities; and to report and make recommendations to the Council concerning these matters."

II. *To change the composition of certain committees.*

(a) *To enlarge the "Committee on Mental Health" and define the composition.*

The Chairman of this Committee recommends that it be enlarged to ten members (from present eight), and that a majority (but not more than six) of members be psychiatrists. For convenience, it would appear desirable to increase the present term of office from four years to five years.

Article XI—Divisional Boards and Committees

Section 3. Divisional Standing Committees

Amend Paragraph 25. *Committee on Mental Health* to read as follows:

"Par. 25. Committee on Mental Health. The Council shall annually nominate to the House of Delegates two members to serve on a Committee on Mental Health and shall nominate the chairman thereof. The Committee shall consist of not more than ten members of whom a majority, but not more than six, shall be psychiatrists, each of whom shall serve for five years. Such nominations shall be made in such manner that the terms of two members shall expire annually."\*\* (The balance of the text of Par. 25 remains unchanged).

(b) *To increase the membership of the "Committee on Program of the Scientific Assembly"*

*The Chairman of the Committee for 1966 recommends that its membership be increased to five members (from the present three), and that consideration be given to having a proper "mix" of the various types of medical practice. Although the chairman suggests that, "an internist, a surgeon, a general practitioner, a pediatrician and an obstetrician-gynecologist" be included, it would not*

\*\* (At the next Annual Meeting of the House of Delegates following the adoption of this amendment, it will be necessary to extend the four-year terms of the then eight incumbent members by one year, and to nominate two new members for the new term of five years. Thereafter, the amendment would be followed as written).

appear wise to spell this out in the Bylaws and thereby exclude other categories of practitioners from serving on the Committee.

#### Article XI—Divisional Boards and Committees

##### Section 5. Duties of Standing Committees

Amend Paragraph 7. *Committee on Program of the Scientific Assembly* to read as follows:

"Par. 7. Committee on Program of the Scientific Assembly. The Council shall annually nominate to the House of Delegates one member of a Committee on Program of the Scientific Assembly for a term of five years. The Committee shall consist of five members, of whom not more than one member shall represent a single type of medical practice, each to serve for a term of five years. The chairman of the Committee shall be the member whose term will expire at the end of his fifth year in office."\*\* (the balance of the present text of Par. 7 remains unchanged).

(c) *To limit the membership of the "Committee on Rural Health".*

*The incumbent chairman of this Committee feels it is "too large to meet effectively and for the work to be done." The present Bylaws specify "not less than five members" and the 1965-66 Committee had twelve members.*

#### Article XI—Divisional Boards and Committees.

##### Section 5. Duties of Standing Committees

The text of Paragraph 29. *Committee on Rural Health* to be amended to read (in lines 3-4): "not more than 8 members and shall nominate the chairman thereof."

III. *To define the eligibility requirements for membership in a Section of the Society's Scientific Assembly and to establish uniformity in this regard among the Sections.*

*On several occasions, the point has come up that in the proposed bylaws of groups of CSMS members requesting authorization to form a Section of the Scientific Assembly, and also in the bylaws of several existing Sections, provision is made to limit membership, all or in part, to CSMS members who also have other specific qualifications; i.e., certification by a specialty board, active membership in another medical organization, etc.*

\*\* (At the next Annual Meeting of the House of Delegates following the adoption of this amendment, two members of the then incumbent, three-member committee will have one and two years remaining to serve, respectively, the member having one year to go becoming chairman. For this reason, and at that Annual Meeting only, it will be necessary to nominate one new member for a three year term; one new member for a four year term; and one new member for a five year term. Thereafter, only one new member would be nominated annually in accordance with the amendment as written).

#### Article VIII—Scientific Assembly

##### Section 2. Meetings

Amend Paragraph 2. *Sections* by deleting entire present paragraph and substituting therefor the following:

##### Par. 2. Sections

(A) *Purposes:* To conduct the work of the Scientific Assembly and for related purposes, the formation of Sections of the Society may be authorized by the House of Delegates.

(B) *Authorization:* Sections of the Scientific Assembly may be created or discontinued by the House of Delegates in accordance with Article V, Section 1. of these Bylaws. Any group of physician members of the Society having a common interest in a recognized branch of medicine may, through application filed with the Council, petition the House of Delegates for authorization to form a Section in that recognized branch of medicine.

(C) *Petition:* A petition to the House of Delegates for authorization to form a Section shall be submitted first to the Council. It shall be in writing and include a roster of interested members, officers pro tem, and a set of bylaws which contain the purposes of the Section and the provisions for granting membership, assessment of dues and the election of officers. Such petition shall be examined by the Council and, if found to be in order, shall be transmitted to the next regular meeting of the House of Delegates with recommendation.

(D) *Membership:* It is the intention of the House of Delegates that the sole qualifications for physician membership in a Section of the Scientific Assembly shall be (1) Active or Life Membership in good standing in the Society, and (2) a bona fide, demonstrable interest in the work of the Section; and that there shall not be other contingent qualifications for such membership. Questions concerning these qualifications shall be resolved by the Council.

(E) *Officers:* Each Section shall have, as officers, a chairman and a secretary and such other officers as the members of the Section may deem advisable, each to be elected by the voting members of the Section during the annual meeting of the Scientific Assembly and to serve for one year. The rights to vote and hold office in a Section shall be limited to physician members of the Society who are in good standing.

(F) *Meetings:* Each Section shall hold a meeting during the course of the annual meeting of the Scientific Assembly and at such other times as the members or officers may deem advisable. The officers of each Section shall arrange the programs for the annual meeting during the Scientific Assembly in accordance with rules established by the Council and the House of Delegates.



## **SUMMARY OF ACTIONS COUNCIL MEETING**

**Wednesday, October 12, 1966**

### **I. Attendance**

Present in addition to the Chairman, Dr. S. J. Martin, were: Drs. Hess, Gardner, W. Martin, Brandon, M. Caplan, Polivy, Rogol, Grendon, Egan, Abbot, Spitz, Hastings, Shepard, Ayres, Nolan, Ciccarelli, Cramer, Fabro, Grant, Petrie, Pelz, Wilson and Roch. Also present: Mrs. Lindquist, Mr. Villano, Mr. Chilcoat (AMA) and Dr. Richards. Absent were: Drs. Bradley, H. Caplan, Weise, Sr., Goldberg and Palomba.

### **II. Routine Business**

#### **Approval Of Minutes**

As printed and distributed, it was VOTED to approve the minutes of the meeting of August 24, 1966.

#### **Life Memberships**

It was VOTED to approve applications for Life Membership received from the following eligible Active Members:

Norman J. Barker, R.F.D. Canton Center, Collinsville (HCMA)

George C. Finley, 50 Farmington Avenue, Hartford (HCMA)

#### **Appointment—Representative To Regional Medical Program**

It was VOTED to appoint William R. Richards, New Haven, as a representative of the Society on a conference subcommittee of state health organizations which will assist the Advisory Board to the Regional Medical Program being planned for Connecticut under the auspices of the Yale University and UConn Medical Schools, as provided for under P.L. 89-239—Heart Disease, Cancer, Stroke, and Related Diseases (DeBakey legislation).

#### **Appointments To CSMS Committee On Public Health**

On recommendation of the PH Committee, it was VOTED to appoint two members of the Society to membership on the Committee for the balance of the 1966-67 term, as follows: Spencer F. Brown, Darien; Howard W. Smith, New Haven. Dr. Brown is currently serving as chairman of the PH Committee's Technical Medical Advisory Committee on Crippled Children, and Dr. Smith as chairman of the similar Advisory Committee on Hearing and Speech.

#### **Resignation—Editorial Committee**

It was VOTED to accept, with regret, the resignation of Hugh F. Lena, New London, as a member of the Editorial Committee of the Journal. Un-

less nominations for replacement of Dr. Lena are received subsequently, the vacancy created by his resignation will be filled by the Nominating Committee for 1967-68.

#### **Date Of Next Meeting**

The next meeting of the Council will be held on Thursday, November 17, 1966.

### **III. Old, New And Special Business**

#### **Report—Delegates To The Council Of New England State Medical Societies**

It was VOTED to accept as information, with thanks, the report filed by Oliver L. Stringfield, Stamford, chairman of the CSMS Delegation to the CNESMS, on the proceedings of the semi-annual meeting of the CNESMS, Portsmouth, N. H., May 21, 1966. In connection with Dr. Stringfield's report, it was VOTED to ask the CSMS Committee on Medical Economics and Insurance to review the CNESMS' Investment and Annuity plans for physicians in the six New England States, and to report to the Council the Committee's valuation of same.

#### **Report—Representative To AMA Conference On Infant Mortality**

It was VOTED to accept as information, with commendation, the report filed by Samuel D. Rowley, Hartford, on his attendance at this Conference, San Francisco, August 12-13, 1966. Dr. Rowley is chairman of the CSMS Committee on Perinatal Morbidity and Mortality, and represented the Society at the Conference. Copies of the report have been distributed to the CSMS Committees on Perinatal Morbidity and Mortality, Maternal Morbidity and Mortality, and Public Health.

#### **Report—Representative To AMA Conference On Rehabilitation**

It was VOTED to accept as information, and with commendation, a report filed by Alexander J. Tuttle, Hartford, on the proceedings of this Conference, Chicago, September 8-9, 1966. Dr. Tuttle attended the Conference as a representative of the Society. Copies of his report have been distributed to the CSMS Committees on Rehabilitation, Aging, and Public Health.

#### **Report—Representative To AMA Regional Conference On Disaster Medical Care**

It was VOTED to accept as information, and with commendation, a report filed by John Shoukimas, Hartford, on the proceedings of this Conference, which he attended as a representative of the Society. Copies of the report will be distributed to members of the CSMS Committee on Disaster Medical Care, of which Dr. Shoukimas is chairman.

#### **Report—Committee On Medicare-Medicaid Experience**

It was VOTED to accept as information copies of the minutes of a meeting of this Committee, held on September 29, 1966. Matters concerning experience with Part B of Medicare (from the physician's standpoint), progress made toward discussing various aspects of Title XIX (Medicaid) with the Welfare Department, and other miscellaneous items relating thereto, were reported on.

Pursuant to receiving this information, Dr. S. J. Martin presented an informal report on discussions held on October 10 between CSMS and Connecticut General liaison representatives. It appears that the over-all experience with Medicare B is heartening to the carrier, although several rather sticky problems remain to be worked out. It was VOTED to accept this report as information, with the expectation that the minutes of the liaison meeting, when finalized, will be distributed to all members of the Council. It was further VOTED to direct the staff to prepare and publish an issue of *Connecticut M.D.*, which will bring this Medicare-Medicaid experience to the attention of the membership.

#### **Report—Committee On Preliminary Study Of Censorship Questions**

Continued from the meeting of August 24, additional sections of the Committee's report on the establishment of a "Judicial Committee" were approved. The staff was requested to prepare a draft of a suitable amendment to the bylaws which would incorporate the provisions approved thus far by the Council. By general agreement, Section "D" of the report, dealing with the mechanism for appeal from disciplinary decisions of the component county medical associations, will be taken up at the next meeting. The Council took cognizance of the amount of time and work which had gone into the preparation of this lengthy report, and it was VOTED to commend Dr. Fabro and his Committee for their efforts.

#### **Reports Of The President-Elect**

E. Tremain Bradley, president-elect, filed informational reports with the Council on meetings he had attended in recent months. The reports and the actions taken thereon follow:

(a) *AMA Public Relations Institute*: Dr. Bradley reported that he had attended portions of the program of the PR Institute, Chicago, August 24-26, and expected that Mr. Villano (who also attended) would inform the Council about the highlights thereof. Acting on his recommendation that the Society study the merits of a direct-billing (individual responsibility) program set up by the Louisi-

ana State Medical Society, the Council VOTED to refer this matter to the CSMS Committee on Third Party Payments for study and report. Pursuant to this action, it was VOTED to also refer to the Third Party Payments Committee, for study and report, a suggestion of the General Manager that the Society might undertake the production and distribution of a standard "disclaimer," which, in cases where assignment of benefits was taken, could be attached to the claim form and state categorically that the acceptance of assignment is not acknowledgement that the payment made is in any way related to the physician's usual (customary) fee.

(b) *Special Meeting of the Council of New England State Medical Societies*: Having attended this meeting, Boston, September 10, Dr. Bradley reported that the president of the CNESMS was anxious to find ways "to make the New England Council more effective," feeling that "it must grow in order to be strong." The meeting also concluded that "there should be more cooperation and communication between the six state medical societies about (joint) activities, particularly *before* changes were made in existing programs or new programs undertaken." It was VOTED to receive this report as information.

Pursuant to this report, the Council received and considered a resolution adopted by the House of Delegates of the Rhode Island Medical Society, which, pointing out that all of the component state societies have either journals or newsletters, expressed objection to a non-society-sponsored publication (*Massachusetts Physician*) being designated as the official publication of the CNESMS, as proposed by its Board of Trustees on September 11. Although no official notice has been received by the Society of this proposal of the New England Council's Board, it was VOTED to inform the three CSMS Delegates to the CNESMS that the CSMS Council does not approve of any single publication being designated as that of the CNESMS, and strongly urges that existing publications of the six state societies be used to disseminate information about activities and programs of the New England Council.

#### **Report—Committee On Third Party Payments**

Filing a report on a resolution (House of Delegates, December 5, 1965) referred to it by the Council for study, the Committee recommended the adoption of a substitute resolution for the one submitted in 1965 by the New Haven County Medical Association. The NHCMA version called for the Council to take steps to attain "the institution of payment for heretofore unpaid services of physicians (furnished) to local and state in-hospital and



out-patient welfare recipients"; to seek "provisions for fee-for-service attendance at privately operated clinics and other medical care facilities"; and to report to the House of Delegates the Council's "accomplishments" in these matters:

It was VOTED to adopt the substitute resolution (with minor amendments) recommended by the Committee, and, together with other information relative to the subject, transmit to the next meeting of the House of Delegates a comprehensive report on the Council's "accomplishments" in the directions called for by the original NHCMA resolution. The substitute resolution reads as follows:

"WHEREAS: In the past, physicians have provided their own organized system of private charity to indigent patients; and

WHEREAS: Governmental and other agencies have assumed this prerogative; therefore be it

RESOLVED: That the House of Delegates of the Connecticut State Medical Society adopt, as official policy, the opinion that the payment of usual fees should be expected by physicians in private practice in return for their professional services, wherever and whenever rendered to any and all patients."

#### **Resolution—Litchfield County Medical Association**

It was VOTED to approve, and to recommend its adoption by the House of Delegates, a resolution submitted by the Litchfield County Medical Association which reads as follows:

"BE IT RESOLVED: That the House of Delegates of the Connecticut State Medical Society express the opinion that, in the best interests of the Connecticut public and the Connecticut medical profession, the Medical School of the University of Connecticut should be oriented toward the education of family doctors, in order to help remedy the shortage of such doctors in the State; and be it further

RESOLVED: That a copy of this resolution be sent to the Governor of Connecticut, the Dean of the University of Connecticut Medical School and the Chairman of its Board of Trustees."

#### **Communication Re Health Education Of Teenagers**

Through communication with President Hess, Morris A. Wessel, New Haven, informed the Council of his hopes that the Society and its component county associations might play an effective role in the areas of meaningful health education and medical counsel for teenagers, particularly with respect to the biological facts of human reproduction, venereal disease, and "unplanned parenthood" facing unwed boys and girls. Expressing

thanks to Dr. Wessel for bringing this matter to the attention of the Council, it was VOTED to request Dr. Hess to bring Dr. Wessel's views, and offer of assistance, to the attention of the Committee on Public Health, and to request that Committee to prepare and submit to the Council a report and recommendations concerning the possible implementation of Dr. Wessel's ideas by the Society and its component associations.

#### **Request—Connecticut Commission On Services For Elderly Persons**

Brought to the Council's attention by the State Commissioner of Health was a request of the Connecticut Commission on Services for Elderly Persons that the Society prepare and submit to the Commission a listing of all physicians in the State who are "competent in the field of geriatrics," such list to be made available to persons age 65 and over who request it from the Commission. Voicing the opinion that, at present, geriatrics is not a recognized "specialty" in medical practice (like pediatrics, surgery, etc.), and that there are few if any disease conditions which are limited to the elderly, it was VOTED to refer the Commission's request to the Committee on Aging for study and report to the Council.

#### **Report—Committee On Postgraduate Education**

Having received a report from the Committee on Postgraduate Education concerning experience with the annual Clinical Congress (including the one held in September, 1966), it was VOTED to accept the report of the Committee and to approve its recommendations as follows:

(a) That no Clinical Congress be planned for or conducted in 1967.

(b) That the Committee continue to evaluate other approaches to postgraduate education in Connecticut which might be implemented as functions of the Society.

#### **Request—Committee On Aging**

Having previously approved the Committee-formulated "guiding principles" on utilization review committees for extended-care facilities, and for the participation of physicians in same, and having authorized the Committee to assist individual facilities or groups of facilities in any area to obtain physicians to serve on such utilization review committees, the Council VOTED to urge the component medical associations and city medical societies to cooperate with the Committee on Aging to obtain interested and qualified local physicians for this purpose. It is understood that the medical associations and societies would only be asked to cooperate when the Committee on

Aging has received an appeal for assistance in obtaining a URC from one or more facilities operating in their respective areas. The request of the Committee was accompanied (as information) by a document titled: "Suggested Guide for Organization and Composition of Community-Based Utilization Review Committees." This document outlines the *modus operandi* for such URC's, the terms of participation for physicians, etc., and has been approved tri-laterally by the Commissioner of Health, the Connecticut Association of Extended Care Facilities and the Committee on Aging.

#### **Semi-Annual Meeting—CSMS House Of Delegates**

It was VOTED to accept, with thanks, the invitation extended by the Council members from the Hartford County Medical Association to have HCMA host the semi-annual meeting of the House of Delegates in the Hartford area during the first week or ten days of December. If possible, the place is to be the Hartford Hilton Hotel, and the date, either the 6th, 7th or 8th of December.

N.B. *The foregoing is a summary of the proceedings and actions of the Council on October 12, 1966. Detailed minutes of the meeting are on file at 160 St. Ronan Street, New Haven, for perusal by any interested member of the Society.*

#### **NEW MEMBERS**

##### **HARTFORD COUNTY**

Temby R. Argall, Glastonbury  
 Stanton H. Avitabile, Glastonbury  
 Eliot B. Barron, New Britain  
 Edwin E. Bowe, Hartford  
 Robert R. Bower, Hartford  
 Donald F. Bradley, Jr., Hartford  
 Charles A. Bucknam, Hartford  
 John T. De Maio, Hartford  
 Robert J. Dobrow, Hartford  
 Ruben Fialkoff, Manchester  
 S. Martin Harwin, New Britain  
 Alkis Ioannides, Hartford  
 Lewis P. James, Jr., Hartford  
 Theodore H. Johnson, New Britain  
 Stanley J. Keating, Jr., Hartford  
 Alan U. Klatsky, Hartford  
 David R. Moloney, Hartford  
 Christopher F. O'Connor, Glastonbury  
 John F. Raycroft, Hartford  
 Mervin Rosenberg, Hartford  
 James E. C. Walker, Hartford  
 H. Kirk Watson, Hartford  
 Thomas J. Zaccheo, New Britain

##### **FAIRFIELD COUNTY**

Stuart H. Bender, Westport  
 Allen C. Chamberlin, Stamford

Thomas D. Cocco, Bridgeport  
 Judith S. Cohen, Stamford  
 Tuula I. T. Fabrizio, Norwalk  
 David N. Franklin, Wilton  
 Jerome J. Klein, Norwalk  
 Samir E. Marrash, Bridgeport  
 Bernard J. Meehan, Newtown  
 Thomas J. O'Neil, Redding  
 Arthur H. Rosenberg, Greenwich  
 Paul L. Schulman, Norwalk  
 John A. Semmelmeier, III, Westport  
 Teunis van der Veen, Norwalk  
 Thomas J. Walsh, Stamford  
 Oliver S. Winter, Norwalk

#### **1967 MEETINGS**

**January 17-19**—New England Postgraduate Assembly will be held at the Statler Hilton Hotel, Boston, Massachusetts. Advance Program will be sent in early December.

**April 12-13**—Seminar on Hospital Infections in Connecticut to be sponsored jointly by the Connecticut State Medical Society, Connecticut Hospital Association, Yale University School of Medicine, the Connecticut State Department of Health and the Communicable Disease Center of the Public Health Service.

**April 25-27**—175th Annual Meeting of the Connecticut State Medical Society to be held at the Hartford-Hilton Hotel, Hartford, Connecticut.

#### **\*PHYSICIANS' PLACEMENT SERVICE CONNECTICUT STATE MEDICAL SOCIETY**

Are you looking for an opportunity to practice in Connecticut? Do you need an associate or partner? Are there towns in your area in need of additional physicians? If your answer is YES to any of the above questions, contact:

**\*Physicians' Placement Service  
 Connecticut State Medical Society  
 160 St. Ronan Street  
 New Haven, Connecticut 06511**

\* No fee for this service.



## **History Of Section On Anesthesiology Of The Connecticut State Medical Society**

**Ralph M. Tovell, M.D.**

1897 Asylum Avenue  
West Hartford, Conn.  
February 17, 1966

Dr. Stevens J. Martin, Chairman  
Dept. of Anesthesiology  
St. Francis Hospital  
114 Woodland Street  
Hartford, Connecticut

Dear Steve:

You, as Chairman of the Committee on History in the State Medical Society's Section on Anesthesia asked me to dig up from memory or from records available to me the circumstances that contributed to the establishment of a Section on Anesthesia. It is for purpose of fulfilling my responsibility to you that I write this letter.

In the early autumn of 1936, it was noted that the Connecticut State Medical Society lacked a Section on Anesthesiology or any affiliated club or organization to correspond to the Horace Wells Club that the dentists of Connecticut had founded in 1894 to honor the memory of the discoverer, demonstrator and proclaimer of the anesthetic properties of nitrous oxide. It seemed appropriate, although too long delayed, that a parallel organization within the ranks of organized medicine might well be established to foster progress in anesthesiology in the State in which Horace Wells was practicing dentistry at the time of his discovery of the anesthetic properties of nitrous oxide. The circumstances of that "giant step forward" have been told and retold many times. I will not recount the events that made Horace Wells an unforgettable figure in the discovery of anesthesia, the modality that with antisepsis and later asepsis made the development of modern surgery possible.

It is noteworthy that in 1936 we were nationally in the process of recovery from the Great Depression of 1929 to 1932. Medicine was feeling the urge to once again progress in terms of organization, education and research leading to, for example, the stirrings toward formation of the American Board

of Surgery with Anesthesiology given temporarily a place with it as the American Board of Anesthesiology both stemming from the Section on Surgery, General and Abdominal, of the American Medical Association. Later the American Board of Anesthesiology was to have independent status with a Section on Anesthesia separate from the Section on Surgery within the A.M.A.'s organization. To get back to my theme, the Connecticut State Medical Society fostered the establishment of a new medical journal to be known as *The Journal of the Connecticut State Medical Society*. The first issue was published in August, 1936, under the able editorship of Stanley B. Weld, M.D., of Hartford.

Progress had been made in another direction, namely the opening of a central office of the Connecticut State Medical Society at 258 Church Street, New Haven, with Creighton Barker, M.D., as Administrative Secretary; Charles W. Comfort, M.D., as Legislative Secretary; Stanley B. Weld, M.D., Secretary on Scientific Work. Jas. R. Miller, M.D., a prominent obstetrician and gynecologist of Hartford was Treasurer of the Society and H. Gildersleeve Jarvis, M.D. of Hartford was the Councillor from Hartford County. The President of the Society in that year, 1936-1937, was Daniel C. Patterson, M.D., of Bridgeport and the Vice Presidents of the Society were Thatcher W. Worthen, M.D. of Hartford and Hugh B. Campbell, M.D., of Norwich. These men and others were all known to me to be interested in progress and improvement in anesthesia and they were in favor of fostering a Section on Anesthesia in the State Society. When the project was brought to the attention of Dr. C. Barker, the Administrative Secretary, I was advised to call a meeting of those primarily interested in formation of such a Section to obtain a vote of a majority of those present requesting that the matter be brought before the Council of the Society.

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DR. RALPH M. TOVELL, Director, Dept. of Anesth., Hartford Hospital, Hartford, Conn.—1936 to 1963, retired.

A meeting for that purpose was convened on March 23, 1937 in the Board Room at Hartford Hospital and on March 24th a letter was written to Dr. Barker requesting formal recognition for a section on Anesthesia in the Connecticut State Medical Society to which Dr. Barker replied on March 30, 1937 that the Connecticut State Medical Society has formally recognized the organization of a Section of Anesthetists in the State Society.

Thus, final approval of our objective was achieved.

Some of a younger generation may ask how achievement of this goal was accomplished apparently so easily and so quickly when physicians limiting their practice to anesthesia in the State could be counted on the fingers of one hand and certainly the primarily interested group did not number more than ten. Prior to formal approval being granted, efforts were made to bring the embryonic specialty to the attention of the medical profession at large and to the attention of individuals in key positions in the State Society specifically. Aside from names already mentioned, many others had been contacted. Among those in Hartford I could mention such stalwarts as Walter R. Steiner, E. R. Lampson, A. M. Rowley, John C. Rowley, Robert L. Rowley, Arthur B. Landry, Benedict B. Landry, Clinton D. Deming, Wm. Dwyer, Howard W. Brayton, Richard C. Buckley, Chas. C. Burlingame, Orin R. Witter, Edward J. Whalen, John A. Wentworth, Claude C. Kelly, Christopher J. McCormack, John B. McCook, and many other equally prominent physicians and surgeons from New Haven, Bridgeport, Greenwich and other towns scattered throughout the State.

In addition, the annual meeting of the Connecticut State Medical Society, held at the Hotel Stratfield, Bridgeport, Connecticut, May 19th and 20th, 1937, featured on its program and immediately following the Presidential Address by Daniel C. Patterson a paper entitled "The Recent Revolution in Anesthesia" (J.C.S.M.S.: 1, 509, 1937) by Harold R. Griffith, Chief Anesthetist, Homeopathic Hospital, Montreal, with Anthony J. Mendillo of New Haven and Jas. R. Miller of Hartford as discussants. At 4 P.M. that same afternoon (Thurs. May 20th 1937) a Section meeting with Leonard F. Del Vecchio, Chairman, presiding. The program included three papers listed as follows: (J.C.S.M.S.: 1, 283, 1937).

1. Preliminary Report on the Reorganization of the Section on Anesthesia, Hartford Hospital, by Ralph M. Tovell, Anesthetist, Hartford Hospital (J.C.S.M.S.: 1, 371, 1937)

2. Chemical Mediation of Nerve Stimuli, Louis Goodman, M.D., Dept. of Pharmacology, Yale University, Ref: J.C.S.M.S.: 1, 473, 1937.
3. Analysis of Peri-dural Anesthesia as Employed at Grace Hospital, Brian C. Sword, Anesthetist, Grace Hospital, New Haven. (J.C.S.M.S.: II, 539, 1938)

Another speaker on the general program was an old friend of mine namely Porter P. Vinson, with whom I had been associated at the Mayo Clinic. He was listed for the May 19th, general session as follows:

The Diagnosis and Treatment of Primary Malignant Disease of the Tracheobronchial Tree, Porter P. Vinson, Professor of Bronchoscopy, Medical College of Virginia, Richmond, Virginia with Norm. F. Verdi of New Haven and Jas. J. Hennessy, Hartford as discussants. J.C.S.M.S.: 1, 351, 1937.

As an aside it is interesting that an article first appearing in the J.A.M.A. Oct. 17, 1936 was republished in May 1937 of the Journal of the Connecticut State Medical Society, page 292. It was entitled "Early Arising From Bed After Operation" Paschoud of Lausanne and Florchén of Frankfurt were mentioned for early work with regard to the method that came to be known by the now familiar term "early ambulation."

On page 9 of an inserted (after page 350) supplement in Vol. I of the J.C.S.M.S. among the Section Officers for 1937-1938, officers of the Section on anesthesia were listed as follows:

Chairman, Leonard F. DelVecchio, 763 Noble Avenue, Bridgeport;

Secretary, Ralph M. Tovell, Hartford Hospital, Hartford.

(Apparently, Dr. B. Sword decided for personal reasons that he could not serve as Chairman.)

The Clinical Congress was held September 21 to 23, 1937 in New Haven, Connecticut. The program (J.C.S.M.S.: I, 441, 1937) lists Dr. Ralph M. Tovell as participating in a Symposium on Caesarean Section. The Section Meeting on Anesthesia was conducted as a Joint Meeting with the American Society of Anesthetists with Dr. L. F. DelVecchio acting as Chairman. The meeting was held in the Auditorium of the Sterling Hall of Medicine at 8:15 P.M. The program was as follows: (J.C.S.M.S.: I, 443, 1937)

Dr. Henry S. Ruth, Philadelphia  
Problems in Resuscitation.

Dr. Louis Goodman, Yale University  
The Chemical Mediation of Nerve Stimuli.  
(J.C.S.M.S.: I, 473, 1937).



Dr. Paul M. Wood, New York City  
Modern Anesthesia in Upper Abdominal Surgery.

Dr. Meyer Saklad, Providence, R. I.  
A Method for the Collection and Analysis of Anesthetic and Surgical Statistics. Published J.C.S.M.S.: II, 119, 1938.

The fact that the meeting was listed as a combined one with the American Society of Anesthetists deserves some explanation. In view of the fact there were so few practicing anesthetists in the State of Connecticut, it was necessary to keep organization as simple as possible. A Chairman and Secretary were named for each year and each served two organizations, the Section on Anesthesia, Connecticut State Medical Society, and the Component State Society of the American Society of Anesthesiologists, Inc. The Section meeting held in New Haven in connection with the Clinical Congress received the support of the American Society in that one of its regular meetings instead of being held in New York City was held in New Haven. The expenses entailed were in great part paid by the parent Society and for that we were grateful. Speakers came from as far away as Philadelphia and Providence and some of those attending came from equally as far away. The support of our efforts to demonstrate the popularity of our meetings was very gratifying. We were given support from an unexpected source. An address was delivered at Trinity College, Hartford, December 11th, 1937 on the occasion of the dedication of a pew end in honor of Horace Wells by the Horace Wells Club of Connecticut. The speaker was Walter R. Steiner of Hartford, Connecticut. His topic was "Horace Wells and His Discovery of Anesthesia." His paper was published in the Journal of Connecticut State Medical Society, II, 525, (Nov.) 1938. An autographed photo of Horace Wells appears in the same issue, II, 524 (Nov.) 1938.

The first meeting for which preparations were made after final approval had been granted May 19, 1937 was the Annual Meeting of the Connecticut State Medical Society held at Hotel Griswold, Groton, Connecticut and again the Section Meeting was a combined one with the American Society of Anesthetists. The program was announced for 4:00 P.M., 2 June 1938, as follows: (J.C.S.M.S.: II, 211, 1938)

1. An Unfavorable Reaction Following the Administration of Avertin. Case Report. George A. Wulp, Hartford.
2. Discussion of Atelectasis. Case Report. Harold F. Bishop, Hartford. J.C.S.M.S. II, 534 (Nov.) 1938.

3. Physiology of Respiration. Howard W. Haggard, New Haven.

This was followed by a dinner meeting at 6:30 P.M. at which B. B. Raginsky, M.D., Montreal, P.Q. was the guest speaker. The title of his paper was: "Hypnotism and its Relation to Anesthesia, with Demonstration." The meeting was attended by approximately 45 for dinner and another 15 or more arrived for the speech and demonstration. Audience participation was a feature of the proceeding and proved to be popular and of keen interest to all attending. J.C.S.M.S. II, 527, 1938.

At the time of the Clinical Congress held September 20, 1938, R. Chas. Adams, M.D. of Rochester, Minnesota presented a paper entitled "Methods of Anesthesia for Operations of the Head and Neck." The paper was published in the Journal of the Connecticut State Medical Society, (II, 544, Nov., 1938).

Thus, anesthesiology was launched in Connecticut as a specialty exciting a growing interest, but without benefit of a constitution, except for acceptance of the Constitution of the American Society of Anesthesiologists, Inc., and Connecticut State Medical Society. There were too few of us to warrant more than a Chairman and Secretary. They doubled in brass for our dual allegiance to Connecticut State Medical Society and the American Society of Anesthesiologists, Inc.

Concurrently, there were stirrings of interest and activity in other directions. A Founder's Group of The American Board of Anesthesiology; a subsidiary of the American Board of Surgery was being considered and the format of written and oral examinations was under study and about to be put to the trial. Rumblings of the need for a new Journal of Anesthesiology could be heard and plans were being made to provide one. Residencies in Anesthesiology were being started and curricula to parallel the examinations being fostered by the American Board of Anesthesiology were being developed. The first resident at Hartford Hospital began training in January 1937. By July 1964, over 200 candidates had been trained or were in the process of being trained and over 100 of these had been certified by the American Board of Anesthesiology. In 1938 rumblings of conflict in Europe were being heard and the hostilities of W.W. II began in September 1939. We were woefully prepared for the cataclysm that was about to descend upon us. We were short of trained personnel, standardized items of equipment and military tables of organization and equipment were either obsolete or non-existent. The efforts of many of us were steered in new directions toward standardization of equipment, preparation of manuals and

the launching of a Journal of Anesthesiology in spite of the fact only 16 per cent of the membership of the A.S.A. voted for it. Those responsible for launching the Journal were not deterred by the vote. It had been planned and decided to go ahead with the project in spite of the vote. The only question was whether or not we formed a private corporation to do the publishing job. Certainly, the membership of the Society had repudiated the idea of assuming responsibility for the featherless fledging. Decision was reached to keep ownership and sponsorship within the American Society of Anesthesiologists, Inc. The membership of the Society may look with pride at the present

format of "Anesthesiology," its circulation of several thousand copies each issue and the profits therefrom. It is true that the many owe a depth of gratitude to a few for disregarding the opinion poll and for keeping the ownership of the Journal within the Society.

The United States became involved in World War II at Pearl Harbor on December 7, 1941 and for most of us, life after that was never quite the same.

Yours sincerely,

RALPH

(Ralph M. Tovell, M.D.)

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### **Regional Conference On Education Of Maladjusted Children**

Public school programs for "socially and emotionally maladjusted children" will be the topic of three Regional Conferences sponsored by the Connecticut Association for Mental Health, the Parent-Teacher Association of Connecticut, and the Connecticut State Department of Education. The Conferences will deal with the provisions and interpretations of Public Act 206 of the 1965 General Assembly. This Act requires all local and regional Boards of Education to "provide special classes, instruction or services" for socially and emotionally maladjusted children starting September 1, 1967.

The Conferences will be held from 3:45 through 8:30 P.M. on December 6th at the Montville High School in Montville, on December 7th at the Central High School in Bridgeport, and on December 8th at the Penny High School in East Hartford. Dr. Thomas Mahan, Jr. will serve as moderator of the conferences.

Reservations for the conferences should be made through the Connecticut Association for Mental Health, 1303 Chapel Street, New Haven, telephone, 787-4228. A charge of \$2.75 will be made for dinner.



# "'Tranquilizer' is not a good word"

**T**HIS classification is psychologically too seductive, pharmacologically too unspecific, and in terms of results not infrequently untrue."<sup>2</sup>

What is a tranquilizer? According to the 24th Edition of Dorland's Medical Dictionary<sup>3</sup> a tranquilizer is "an agent which acts on the emotional state, quieting or calming the patient without affecting clarity of consciousness."

Defining a drug by its effects, however, can be misleading. The same effects by which the dictionary defines a tranquilizer have sometimes been seen after administration of a sedative — or, for that matter, a placebo.

Ambiguous though the term may be, it appears to be here to stay. The 1966 edition of the Physicians' Desk Reference<sup>4</sup> lists 42 tranquilizers indicated for treatment of anxiety and apprehensive states.

## 'Tranquilizers' have differences in action, differences in effect

Although all tranquilizers are intended to calm anxious patients there are differences in their actions — and in their effects. They have been divided into three categories — the rauwolfia group, the 'minor' tranquilizers, and the phenothiazines.<sup>5</sup>

Although the tranquilizing effect of rauwolfia has been known for centuries, its use as an antipsychotic agent in current practice has diminished.<sup>5</sup>

A 'minor' tranquilizer is often prescribed to achieve more than one effect. Thus, besides being tranquilizers some of these compounds may be muscle relaxants, antihistaminics with some calming action, anticholinergic sedatives, or antispasmodics.<sup>5</sup>

The phenothiazines are considered 'major' tranquilizers because they alter psychotic behavior.<sup>1</sup> This classification may have done them more harm than good because it implies that the phenothiazines should be reserved for the more

severely disturbed. This is not necessarily true.

## The phenothiazines — and the problem of sedation

One of the problems of prescribing phenothiazines for ambulatory patients has been the fear that excessive sedation will impair the patient's ability to function. This, however, is less of a problem with some of the phenothiazines.

"Clinically they may be differentiated primarily in terms of their potency and the extent of their sedative effect, which appear to be inversely proportional. That is, the least potent, the one which is used in highest dosage, chlorpromazine, is the most sedative, while the reverse holds true for fluphenazine."<sup>6</sup>

In a recent report on various studies conducted over several years evaluating 360 patients treated for anxiety and stress with seven phenothiazines, this inverse relationship of potency to sedation was confirmed.<sup>7</sup> Also under consideration was the degree to which the particular phenothiazines neutralized anxiety (the angolytic index). Interestingly enough there was, again, an inverse relationship. The most sedative of the phenothiazines appeared to be the least active in neutralizing anxiety. Flu-

phenazine, one of the least sedative, on the other hand, was found to be most effective in relieving anxiety.<sup>7</sup>

RELATIVE SEDATIVE AND ANGOLYTIC INDICES OF PRINCIPAL PHENOTHIAZINES\*

| DRUG            | SEDATIVE INDEX | ANGOLYTIC INDEX | BASED ON STANDARD DOSE OF |
|-----------------|----------------|-----------------|---------------------------|
| Chlorpromazine  | 100            | 15              | 25 mgs.                   |
| Trifluoperazine | 100            | 15              | 25 mgs.                   |
| Thioridazine    | 90             | 17              | 25 mgs.                   |
| Perphenazine    | 15             | 25              | 4 mgs.                    |
| Carphenazine    | 25             | 25              | 25 mgs.                   |
| Trifluoperazine | 3.3            | 95              | 2.0 mgs.                  |
| Fluphenazine    | 3.5            | 100             | 2.5 mgs.                  |

\*adapted from Sainz<sup>7</sup>

## Prolixin is therapeutically effective without excessive sedation

When used as a 'tranquilizer' in general medical practice, in many patients Prolixin (Squibb Fluphenazine Hydrochloride) suppresses anxiety, but not normal activity. These two features are of particular importance to patients who must be able to live and work without their normal daily activities being restricted.

Because of its longer duration of action, Prolixin, in doses of as little as one to three milligrams in adults, generally taken once a day, is effective in maintaining many patients free of their symptoms of anxiety and tension.

**Contraindications:** Do not use with high doses of hypnotics or in patients with subcortical brain damage. Use with caution in patients with a history of convulsive disorders. Severe reactions may occur in patients with idiosyncrasy to other centrally-acting drugs, and severe hypotension may occur in patients with special medical disorders, e.g. mitral insufficiency and pheochromocytoma.

**Precautions:** Effects of atropine, anesthetics and C.N.S. depressants may be potentiated. Hypotension may occur in patients undergoing surgery. Do not use epinephrine for treatment of the hypotensive reactions which may appear in patients on phenothiazine therapy.

**Side Effects:** Extrapyramidal reactions, allergic skin reactions, the possibility of anaphylaxis, drowsiness, visual blurring, dizziness, insomnia, nausea, anorexia, salivation, edema, perspiration, dry

mouth, abnormal lactation, polyuria, hypotension, and jaundice and biliary stasis may occur. Routine blood counts are recommended to determine possible blood dyscrasias; if symptoms of upper respiratory infection occur, discontinue drug and institute appropriate therapy.

**Available:** 1 mg. tablets. Bottles of 50 and 500.

For full prescribing information, see package insert

**References:** 1. Simpson, G.M.: Postgrad. Med. 39:557, 1966. 2. Freyhan, F.A.: Am. J. Psychiat. 115:577, 1959. 3. Dorland's Illustrated Medical Dictionary, ed. 24, Philadelphia, W. B. Saunders Co., 1965, p. 1603. 4. Physicians' Desk Reference, 1966, Oradell, N.J., p. 310. 5. Cohen, S.: Northwest Med.: 65:197, 1966. 6. Detre, T., and Jarecki, H. Connecticut Med. 25:553, 1961. 7. Sainz, A.: Psychosomatics 5:167, 1964.

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'The Priceless Ingredient' of every product is the honor and integrity of its maker.

# Letters To The Editor

## To The Editor:

Do you believe that at this time vectorcardiography has any advantages over conventional electrocardiography in clinical practice? Thank you.

Yours truly,

S. A. ROSE, M.D.,  
Director, Heart Station  
The Stamford Hospital

Stamford, Connecticut

Dear Dr. Rose:

Some years ago we asked ourselves the following question. Is the heart really a dipole so that it can be treated mathematically as Augustus Waller suggested in 1888 and Einthoven attempted by his mathematical derivation?

We did this by establishing the field function on the surface of the body.\* We found several unexpected things. First throughout most every instant of the QRS complex in the normal man there was a maximum positive and a maximum negative region, but in many abnormal patients and in some instants of the normal there was more than one negative and one positive pole, often two separate positive poles or two negative poles or both. This was unsettling as far as the dipole concept was concerned because there was no single electrical axis.

Further unsettling to the vector concept was first that the equipotential lines in the negative and positive distribution were not symmetrical but very distorted, making the dipole concept untenable.

Another unsettling finding was that when we drew a line joining the maximum negative to the maximum positive pole as if this represented the vector, it was far away from the axis calculated by the Einthoven equation.

Needless to say this meant to us that a vector did not exist and that if one tried to make one it did not correspond to the ideal one as envisioned by Waller and Einthoven. This brings me to vectorcardiography. If the heart is too complex to have one vector what should we think of the vectorcardiogram as giving us either theoretical or practical information.

The vectorcardiogram is a curve resulting from the electromechanical union of two leads. The vectorcardiographers have for a long time not settled on the ideal two leads. This meant that the records they were getting did not correspond with pathology and that what they had was a graph which needed to be elucidated by clinical pathological correlations and experimental methods much as our knowledge of the electrocardiogram evolved. Thus far the vectorcardiogram has uncovered almost no new information which is not recognizable to the expert electrocardiographer.

There is no reason why the instrument should not be an experimental tool to determine what the vectorcardiogram looks like in various types of cardiac pathology produced by nature and also by experiment. But in clinical practice it has not found any serious uses up to now.

Our knowledge of the electrocardiogram has developed

after going through empirical and experimental study which the vectorcardiogram has yet to do and it is reliable as a measure of what is going on at the cellular level and also for localizing injury involving epicardial and outer myocardial layers.

To be sure there are silent areas in the myocardium and subendocardial layers. But knowledge of these silent areas will be expected to be as blank in the vectorcardiogram as they are in the electrocardiogram. The reason for this is probably that there is much cancellation of potentials in the heart as one would expect in such a complicated organ with fibers running in many directions.

Sincerely,

LOUIS H. NAHUM, M.D.

New Haven, Connecticut

\* Nahum, L. H. Electrical correlates of the cardiac cycle. Fulton's physiology. Wm. B. Saunders 1955. Chap. 33, 633-682.

*Letters to the Editor are welcome and will be published for informative and educational purposes as space permits. As with other material which is submitted for publication, all letters will be subject to the usual editing. Address all correspondence to: THE EDITOR, CONNECTICUT MEDICINE, 160 St. Ronan Street, New Haven, Connecticut, 06511.*

## Advertisements Worth Reading

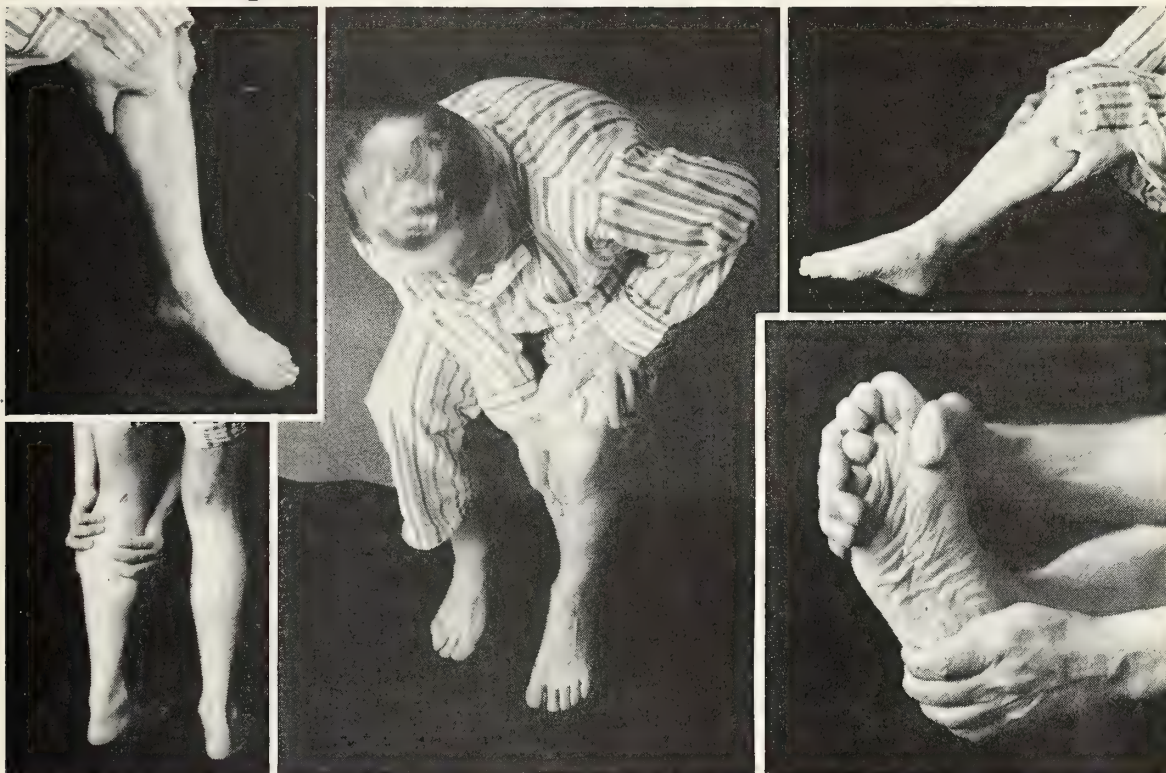
It is virtually impossible to keep up with reports on all the new drugs and other technical as well as non-technical products available to the physician. No doctor has the time to expose himself to all the available journals that contain this information. The type of advertisement that appears in CONNECTICUT MEDICINE helps to keep our readers abreast of the new products.

Many of us have become irritated by the banal material we see on television such as the anvil in the headache or the mechanical stomach with the faucet dripping acid. Perhaps this has resulted in a very generalized antagonism against any and all kinds of advertising. This is unfortunate. The type of advertising found in this journal we believe to be worthwhile or it would not be accepted.

The revenue that comes from our advertisers is not only appreciated but also makes possible the publication of CONNECTICUT MEDICINE at a reasonable cost to each member of the Connecticut State Medical Society. But of very great importance and value is the basic information that can be found in the pages they provide.



# Night Leg Cramps... Frequent Bedfellow in Diabetes, Arthritis, and Peripheral Vascular Disorders\*



"Nocturnal cramps occurring in the calf muscles and small muscles of the feet have been encountered in a significant number of diabetic patients."<sup>1</sup>

"... nocturnal cramps may be the presenting symptoms of patients with arteriosclerosis obliterans, deep thrombophlebitis, varicose veins, osteoarthritis..."<sup>2</sup>

**now...specific therapy for night leg cramps**

# QUINAMM<sup>TM</sup>

Consistently effective, QUINAMM provided complete relief in 94% of 200 patients studied, many of whom were severe cases refractory to other medication.<sup>3</sup> Your prescription for one tablet at bedtime often controls painful night cramps with the initial dose... helps restore restful sleep.

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**QUINAMM Composition:** Each white, beveled, compressed tablet contains: Quinine Sulfate 4 grains (250 mg.), Aminophylline 3 grains (200 mg.). **Precautions:** Aminophylline may produce intestinal cramps in some instances, and quinine may produce symptoms of cinchonism, such as tinnitus, dizziness, and gastrointestinal disturbance. Discontinue use if ringing in the ears, deafness, skin rash, or visual disturbances occur. **Contraindication:** QUINAMM is contraindicated in pregnancy because of its quinine content. **Dosage:** One tablet upon retiring. Where necessary, dosage may be increased to one tablet following the evening meal and one tablet upon retiring. **Supplied:** Bottles of 100 and 500 tablets. **Caution:** Federal law prohibits dispensing without prescription. **References:** 1. Shuman, C.: Am. J. Med. Sci., 225:54, 1953. 2. Perchuck, E., et al.: Angiology, 12:102, 1961. 3. Rawls, W. B., et al.: Med. Times, 87:818, 1959.

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**How long will  
it take her  
to recover from  
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**Does she really care?  
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*Adequate dosage is important: Prescribe Alertonic—  
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*And for your patient's sake, prescribe Alertonic  
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Each 45 cc. (3 tablespoonfuls) contains: alcohol, 15%; pipradrol hydrochloride, 2 mg.; thiamine hydrochloride (vitamin B<sub>1</sub>) (10 MDR\*), 10 mg.; riboflavin (vitamin B<sub>2</sub>) (4 MDR), 5 mg.; pyridoxine hydrochloride (vitamin B<sub>6</sub>), 1 mg.; niacinamide (5 MDR), 50 mg.; choline,† 100 mg.; inositol,† 100 mg.; calcium glycerophosphate, 100 mg. (supplies 2% MDR for calcium and for phosphorus) and 1 mg. each of the following: cobalt (as chloride), manganese (as sulfate), magnesium (as acetate), zinc (as acetate), and molybdenum (as ammonium molybdate).

\*Multiple of adult Minimum Daily Requirement supplied.

†The need for these substances in human nutrition has not been established.

**Indications:** 1. Functional fatigue such as that often associated with: a depressing life experience or stressful time of life; advancing years; convalescence; limited activity or confinement. 2. Poor appetite and vitamin-mineral deficiency as they occur in: patients having faulty eating habits; geriatric patients who are losing interest in food; patients convalescing from debilitating illness or surgery.

**Dosage:** Adults, 1 tablespoonful; children (over 15 years old), 1 to 2 teaspoonfuls; children (4 to 15 years old), 1 teaspoonful. To be taken three times daily 30 minutes before meals.

**Contraindications:** As with other drugs with CNS stimulating action, Alertonic is contraindicated in hyperactive, agitated or severely anxious patients and in chorea or obsessive compulsive states.

**Side effects:** Reports of overstimulation have been rare. Patients who are known to be unduly sensitive to the effects of stimulant drugs should be observed carefully in the initial stages of treatment.

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# WOMAN'S AUXILIARY

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The 23rd Conference of the Woman's Auxiliary to the American Medical Association for State Presidents, Presidents-elect, National Officers and Chairmen, was held October 2-4 in Chicago at the Drake Hotel. Attending from Connecticut were Mrs. John D. O'Connell, President; Mrs. Anthony Cipriano, President-elect; and Mrs. Norman Gardner, a director of the National Board of the Woman's Auxiliary.

The Eastern Regional Workshop of the Woman's Auxiliary to the A.M.A. was held October 10-11 in New York City. The State President and President-elect attended these meetings with the following Chairmen: Mrs. Norman Barker, A.M.A.-E.R.F.; Mrs. Dewey Katz, Community Service and School Health; Mrs. William R. Richards, Legislation; Mrs. David Waskowitz, Health Careers.

Their reports will be in the next issue of the *Quarterly* and will be of much help and interest to members in every county of the State. There is much that YOU as a doctor's wife can do through your County and State Auxiliary. Join if you have not, you *are* the AUXILIARY, without you it cannot exist and all the conferences in the world will not help if there is no one to carry out the aims of the Auxiliary and A.M.A. Once you have joined, choose the project you are most interested in and work at it. The National Board is now offering us "Package Programs" which are to help you present programs pertaining to health problems in your community. They contain lists of films, pamphlets, and even a speech written by an authorized physician. Some of the subjects covered are "Venereal Disease in Teen-Agers," "Immunization," and "Youth Health and Fitness."

## THIS IS OUR STORY . . .

*When Organized*—May 26, 1922, in St. Louis, Missouri, by Mrs. Samuel Clark Red and Dr. Edward Carey of Texas. Twenty-four women from

nine states attended the organization meeting. State auxiliaries already organized at that time—Texas, Oklahoma, South Dakota, Maine, Minnesota and Montana.

*Why Organized*—According to its bylaws the objects of the auxiliary are: 1) to assist the American Medical Association in its program for the advancement of medicine and public health; 2) to coordinate and advise concerning the activities of constituent auxiliaries, and 3) to cultivate friendly relations and promote mutual understanding among physicians' families.

*Legislative Body*—House of Delegates made up of national officers and chairmen, state presidents and state delegates on the basis of number of members.

*Board of Directors*—Elected and appointed officers carry out auxiliary policy determined at annual sessions of the House of Delegates.

*National Committees*—Program extension and special committees include Health Careers, Rural Health, Mental Health, Safety-Disaster Preparedness, Legislation, Community Service, International Health Activities, Homemaker Service, Meals-on-Wheels, Volunteer Friendly Visitor Training and American Medical Association Education and Research Foundation. Chairmen make suggestions on priority projects to state chairmen who in turn pass them on to county chairmen.

*Publications*—Official magazine, *MD's Wife*, is issued bimonthly. Annual *Minutes and Reports*, annual *Directory* of officers and chairmen and the *Direct Line*, a newsletter for county and state auxiliary leaders, also are published.

*Medical Advisors*—All projects and programs must be approved by county medical society advisors. National and state advisors suggest emphases.



*Auxiliary Representatives* serve as members or participate in activities of such bodies as:

President's Committee on Employment of the Handicapped  
Division of Health Mobilization, U. S. Department of HEW  
Home Health Agency Advisory Committee to the Social Security Administration  
Women's Activities Conference of the National Safety Council  
National Citizens Committee for Educational Television  
Committee on Careers, National League for Nursing  
National Health Council  
Advisory Committee for Health Careers, National Health Council.  
National Council for Homemaker Services  
National Voluntary Health Agencies  
State and County Welfare Boards  
State Governors' Commissions and Committees.

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## Special Notice

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### THE YALE MEDICAL SOCIETY

will present a lecture on

### CYTOCHLEMIC ASPECTS OF ELECTRON MICROSCOPY

by Dr. Russell J. Barrnett

Professor of Anatomy

**Tuesday, November 20, 1966**

at 5:00 P.M.

Mary S. Harkness Auditorium

333 Cedar Street, New Haven

This lecture is open to all who may be interested.

### A TEACHING PROGRAM IN ADMINISTRATIVE PSYCHIATRY

The Department of Epidemiology and Public Health at the Yale University School of Medicine has been awarded a three-year grant of \$74,805 by the Maurice Falk Medical Fund. The program proposes to train psychiatrists in administrative and management skills so that they will be able to supply the leadership required by the burgeoning of programs throughout the country in comprehensive community mental health services. The program will draw on the facilities and resources not only of the Department of Epidemiology and Public Health but also of the Connecticut Mental Health Center, the State Department of Mental Health, and related University departments.

The grant will make possible a program director for planning and development of the syllabus of teaching and training. Inquiries should be directed to: Jules V. Coleman, M.D., Mental Health Section, Department of Epidemiology and Public Health, Yale University School of Medicine, 60 College Street, New Haven, Conn. 06510.

### PLACEMENT OPPORTUNITIES

G.P. to specialize in psychiatry. Psychiatric residencies available in community-oriented mental hospital. Associated with Yale Depts. of Psychiatry and Neurology. Opportunities for training in fields of special interest, arrangements can be made to be accepted for degrees in community health and hospital administration at Yale. Psychoanalytic training available at Western New England Psychoanalytic Institute. Salary \$12,000 yearly under NIMH grant, excellent fringe benefits. All particulars and references included in first letter. Contact Connecticut Valley Hospital, Box 351, Middletown, Conn. 06458. An equal opportunity employer.

**CLINICAL PHARMACOLOGIST** — Physician who wants to combine medical knowledge, scientific inquisitiveness and administrative skills. Highly desirable are previous experience in pharmaceutical industry, background of private practice and some type of specialized medical training, although a strength in one area may outweigh a lack in others. As a member of Research Div., he will be active in planning new medicinal research programs. Between 10 per cent and 20 per cent of the time, the physician will be on scientific field trips or attending various professional meetings, but will rarely be gone for more than three consecutive days. Members of Clinical Pharmacology Dept. are encouraged to publish scientific papers based on their own studies. Contact: D. V. Vines, Personnel Mgr., Chas. Pfizer & Co., Groton, Conn. 06430.

**INTERNIST** — The Chapel Medical Group is looking for an internist. This is a three-man group and they have a regularly visiting specialist consultant staff with modern clinic facilities, with scheduled training and vacation periods. The starting salary is \$15,000-\$18,000, with a partnership in one year. Please submit qualifications to Chapel Medical Group, 1308 Chapel Street, New Haven, Conn. 06511.

### PLACEMENT WANTED

**INTERNIST**—29 years of age, married, Board eligible. Would like to practice in either a solo or partnership situation within easy traveling distance of New York.

**PEDIATRICIAN** — 37 year old Board eligible pediatrician with background in general pediatrics and pediatric oncology desires to associate with other pediatricians in New Haven area. Military obligations completed, applied for Connecticut license.

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## In Memoriam

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**Boguniecki, Stanley J.**—Meriden, Harvard Medical School, 1940. Dr. Boguniecki had been a general physician and surgeon in Meriden for over 20 years. During World War II, he entered the U. S. Navy and served in the South Pacific Theater of Operations with a Marine Landing Base Squadron. He was discharged in 1945 with the rank of full commander. He was a member of the U. S. Naval Reserve. He was a member of the surgical staff of the Meriden Hospital since 1946. Dr. Boguniecki was a member of the American Academy of General Practice, the American Medical Association, the Connecticut State Medical Society, the New Haven County Medical Association, and the Meriden Medical Society. He was a member of the board of directors of the YMCA and the Visiting Nurse Association in Meriden. Dr. Boguniecki died September 12, at the age of 52.

**Carrozzella, John C.**—Wallingford, Long Island Medical School, 1928. Dr. Carrozzella had practiced medicine in Wallingford for 37 years. He was a member of the students army training corps in World War I. Dr. Carrozzella was a Connecticut State Police surgeon, a member of the staff of St. Raphael's Hospital, New Haven, and the Veterans Memorial Hospital in Meriden. He was a former member of the Wallingford Board of Education. He held memberships in the American Academy of General Practice, the American College of Allergists, the American Medical Association, the Connecticut State Medical Society, the New Haven County and City Medical Associations, the Meriden Medical Society, and many civic organizations. Dr. Carrozzella died August 14, at the age of 66.

**Magyar, Steven P.**—Hamden, LaVal Medical College, Quebec, Canada, 1943. Dr. Magyar had practiced medicine in New Haven since 1948 and was a lecturer in anatomy at the Yale School of Medicine for the past four years. During World War II, Dr. Magyar was with the U. S. Public Health Service at the Marine Hospital on Staten Island as assistant chief of surgery. He was a member of the New York Academy of Arts and Sciences, the American Medical Association, the Connecticut State Medical Society, the New Haven County Medical Association, and the New Haven City Medical Association. Dr. Magyar died August 23, at the age of 49.

**Chernaik, Samuel**—New Britain, Jefferson Medical College, 1916. Dr. Chernaik was a prominent general practitioner in New Britain for over 30 years. He was attending physician at New Britain General Hospital and New Britain Memorial Hospital. He was a member of the New Britain Medical Association, the Hartford County Medical Association, the Connecticut State Medical Society, the American Medical Association, and the American College of Physicians. Dr. Chernaik died September 27, at the age of 72.

**Moyle, Henry B.**—Canton, University of Toronto Medical School, 1910. Dr. Moyle had served as director of the Hartley-Salmon Clinic in Hartford for 25 years. During World War I, Dr. Moyle served as a captain in the Royal Army Medical Corps. He was a consulting psychiatrist for the Newington Hospital for Crippled Children. He was a Diplomate of the American Academy of Neurology and Psychiatry, a Fellow of the American Psychiatry Association, the American-Ortho-Psychiatry Association, and the American Academy of Child Psychiatry. He was a member of the American Medical Association, the Connecticut State Medical Society, and the Hartford County Medical Association. Dr. Moyle died August 26, at the age of 83.

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### 1966 Diabetes Detection Drive November 13-19

Diabetes Week will be observed November 13-19, marking the eighteenth annual diabetes detection drive in search of hidden diabetics.

The rapid rise in the prevalence of diabetes presents the medical profession with an exceptional opportunity to perform a valuable service both to the public and to the many individuals who have diabetes and do not know it. Estimates place the number of people in this category at well over a million and a half, and new cases are now being diagnosed at a rate of at least 250,000 per year.

The earlier diabetes is diagnosed and brought under appropriate treatment the better the prognosis. In most cases early detection (preferably in the asymptomatic stage) makes it possible to control the condition effectively so that the cooperative patient has a reasonable expectancy of living an abundant and useful life.



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## NEW BOOKS IN REVIEW

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**FERMENT IN MEDICINE: A Study of the Essence of Medical Practice and of Its New Dilemmas.** Richard M. Magraw, M.D., Editor; with a chapter on Automation in Medicine written in collaboration with Daniel B. Magraw, M.B.A. The W. B. Saunders Co., Philadelphia, 1966. 272 pp. \$6.50.

Reviewed by: LOUIS H. NAHUM

We certainly are in a transition phase of medical practice and it appears that the doctor himself has not taken time to see it, evaluate it and decide what his role now really is. Dr. Magraw, a professor of Medicine and Psychiatry at Minnesota, has undertaken this herculean job and has done it well. His thesis is that there has been an explosive increase in biological knowledge and rapid technological advances that have changed the patterns of professional activity and the structure of medical institutions which have somehow bypassed the personal physician.

While this has been going on and institutional practice has been rising and group practice developing, the doctor himself has continued in his old philosophy of personal physician. He has been uncertain what to do about the medical social upheaval and has acted either by denying that changes are really here or resisting them until resistance turned futile as in the case of the Medicare law.

The doctor now is forced to redefine the care of medical activity, what the practice of medicine really is and what is the central medical task. Is it just the care of the patients' sickness. Is free choice of physician really necessary or helpful in medical care. Is the doctor-patient relationship significant in individual well being? Dr. Magraw clearly describes how much of medicine is changing from an individual to a cooperative venture, the evolution of the hospital and its impact upon medicine. He deplores that there is no systematic presentation in medical schools of the nature and purpose of medical practice. The emphasis upon biomedical research and care of diseases in medical institutions has made the care of the sick person, in contrast to his disease, almost non-existent.

Dr. Magraw believes in the important role of the personal physician as the primary and continuing link between family and all specialized resources for medical care. He worries about the lack of provision for paying for comprehensive personal care in medicine. Many prepayment plans pay a doctor for one job, the care of a disease, and expect him to do another job free, that is the care of the patient as well. Comprehensive personal care has always been a "give-away" item or a loss-leader in the medical market. Doctors are paid for doing immediate things, examination, technical tests, operations, but there is no way of being paid for personal care. It is given free.

Detection and management of latent or presymptomatic disease, if it were to develop, would strongly support a pattern of practice on personal ongoing responsibility by a physician for individual patients. If a physician could be adequately paid for this type of practice, there would be no danger of the family physician disappearing. It would pro-

duce a new family physician with training programs to help men acquire genuinely professional skill in the coordination of medical care.

Whether one agrees with this whole thesis, it is a book to be read by all physicians.

**DISEASES OF THE NEWBORN.** Alexander J. Schaffer, M.D. W. B. Saunders Company, Philadelphia and London, Second Edition 1965. 1023 pages, illustrated \$22.00.

Reviewed by: ORVAN W. HESS

This book is the second edition of a textbook dealing with the symptomatology and treatment of disease of the neonate. Clinicians will find this 1023 page treatise a useful reference book covering the general aspects of the normal and abnormal newborn, disorders involving the various organ systems, as well as common problems associated with nutrition and infections. There is recorded an abundance of information accumulated by the author during many years of careful observation and evaluation of the neonate. It is well illustrated with an appendix which includes principles of infant care, methods of resuscitation, management of erythroblastosis and other important diseases encountered among infants. In an era of such an explosion of new knowledge and changing concepts any attempt to provide a complete and definitive text is an extremely difficult task. The specialist or researcher who may be stimulated to pursue a specific subject in depth, will find excellent references have been listed as an aid to further investigation. The content of the book includes abundant referral to numerous pertinent disciplines. Obstetricians and pediatricians, with their necessarily overlapping interest and responsibility in neonatology, should find this textbook valuable.

**PREIMPLANTATION STAGED OF PREGNANCY.** Ciba Foundation Symposium. G. E. W. Wolstenholm and M. O'Connor. Little, Brown and Co., Boston Massachusetts, 1965. 430 pp. with 153 illustrations. \$13.50.

Reviewed by: C. D. DAVIS

This book contains the scientific proceedings of another Ciba Foundation Symposium. It brings together twenty-six scientists, eleven of whom were from the United States. There were sixteen different presentations, including such diverse subjects as ultrastructural changes in the ova during fertilization, electron microscopic study of the blastocyst, sperm penetration of the zona pellucida, maternal factors and development of the rabbit ova, etc. A discussion after each presentation is given as well as a general discussion at the conclusion of the conference.

This work contains much of interest to the scientist working in the field of preimplantation physiology. Much of it is far beyond my comprehension and, I am sure, is a book that would only be interesting and helpful to a very select circle of people.

**FIVE CONGENITAL CARDIAC DEFECTS. A Study of the Profile and Natural History. Edited by James W. DuShane, M.D., and William H. Weidman, M.D. The American Heart Association, New York, 1965. 52 pp. \$2.50.**

Reviewed by: HERBERT LEVINE, M.D.

The American Heart Association Monographs on specific aspects of cardiovascular diseases are generally of high caliber, and the present volume, the twelfth, is no exception. The design is clearly outlined in the foreword as a retrospective study of the natural history of five important congenital cardiac lesions. Aside from its intrinsic value, the material presented is also intended to serve as a guide and baseline for future studies of both a prospective and a retrospective nature. Five centers participated, and each contributed a stated number of proven cases studied in specific periods. The diagnostic criteria are stated in a definitive and comprehensive manner in the foreword. The text consists of analyses of aortic stenosis, atrial septal defects of both primum and secundum types, pulmonic stenosis, and ventricular septal defect. The cases are discussed from the standpoints of symptoms, signs, electrocardiography, roentgenography, and hemodynamics, and changes in these parameters over the period of observation are stressed.

A number of interesting observations are made in the text. One is accustomed to think of patients with aortic stenosis and experiencing angina or syncope as having a poor prognosis and being likely to die suddenly. In the small series reported here the mortality rate was lower and the survival period longer than in previous ones. The tendency for aortic stenosis to remain stable hemodynamically for long periods of time was also not observed here. In contrast, however, the hemodynamic stability of atrial septal defects of the secundum type was demonstrated in the present series.

All the analysts from the five participating institutions are aware of methodological limitations, and approach the analysis of data with caution. In this era of rapid technical advance in therapeutic and diagnostic modalities, studies such as the present one provide invaluable data for the assessment of diagnostic criteria and therapeutic results.

**DISORDERS OF CARBOHYDRATE METABOLISM IN INFANCY. Vol. II in Series Major Problems in Clinical Pediatrics. Marvin Cornblath, M.D., and Robert Schwartz, M.D. The W. B. Saunders Company, Philadelphia and London, 1966. 271 pp. Illustrated. \$8.50.**

Reviewed by: JEROME T. COMBS

This monograph is a logical presentation of current concepts of normal and abnormal carbohydrate metabolism in the infant. The eminently qualified authors present their discussion with a great wealth of references (over 600) and in a straightforward, concise manner which is judged readily assimilable. The generous use of subtitles allows easy reference to topics covered in each chapter. The use of bold type for important concepts of diagnosis or therapy serves to increase the usefulness of the monograph as a quick guide for the practicing physician.

The monograph is divided into five parts; Introduction, Problems of the Newborn and Neonate, Hereditary Meta-

bolic Disorders, Hypoglycemic Syndromes of Infancy, and Sugar Malabsorption Syndromes.

The introduction reviews normal carbohydrate metabolism, the metabolic adjustments of pregnancy and carbohydrate homeostasis in the newborn. The review of normal carbohydrate metabolism is too brief. It could have been expanded considerably without risking the confusion or boredom of the practicing physician. The authors' discussion of maternal-fetal carbohydrate metabolism is more than adequate and the chapter on carbohydrate homeostasis provides an excellent foundation for their elaboration of abnormal states.

Part two presents a practical discussion of the hypoglycemic newborn. The chapter on the infant of the diabetic mother appropriately begins with a quotation from Farquhar, "These infants are remarkable not only because like foetal versions of Shadrach, Merhach and Abidnego, they emerge at least alive from within the fiery metabolic furnace of diabetes mellitus . . ." and goes on to be one of the clearest presentations of the problems of these infants that one might find anywhere. The chapter on transient hypoglycemia in the newborn has many helpful tables, which include the symptoms of these infants, the differential diagnosis and a reasonable and concise outline of therapy. We would judge this chapter to be most useful to the pediatrician or family physician who occasionally finds himself faced with the emergency care of a newborn with symptomatic hypoglycemia.

The hereditary disorders covered are abnormalities of glycogen metabolism, galactosemia and fructose intolerance. The fact that over half of the 155 references cited in this section are to articles published since 1960 is evidence that the authors give a current account of the material.

The first chapter of the part dealing with hypoglycemic syndromes covers general considerations. While most of the information is of value, one questions the worth of a table listing the causes of hypoglycemia in eleven children. The table entitled "hypoglycemic work-up" is also an exception to the general value of the tables and figures in the monograph. This table is poorly organized, has internal inconsistencies, is confusing and therefore serves no useful function. One has to have read the book before beginning to understand the table. The chapter on specific hypoglycemic syndromes is well done with one exception. The term "infant giants" is used by the authors without published reference and it is not readily apparent that the term refers to familial neonatal hypoglycemia resembling foetopathica diabetica. One therefore may be left without an adequate description of the syndrome that they sometimes call "infant giants".

The final part of the book, which includes a discussion of disorders of carbohydrate absorption and digestion, special carbohydrate diets and a listing of the carbohydrate content of many common foods, should prove useful to the practicing physician.

The monograph is a worthwhile addition to the library of pediatricians and general practitioners as a valid guide for the management of infants and children with disorders of carbohydrate metabolism. The volume is beautifully bound and printed on high quality paper. Unfortunately the price of the book will discourage its wide distribution among pediatric house staff who would find it most useful.





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## Adverse Reactions To LSD

What kind of person takes LSD without medical supervision? Does he really suffer as many ill effects as have been claimed?

Reporting on what they believe to be one of the largest groups of LSD-related adverse reactions studied to date, investigators at the University of California, Los Angeles, describe 70 persons treated after unsupervised LSD administration. The report appears in the current (August 8) Journal of the American Medical Association.

The patients were "predominantly single, white, male and young (average age, 21)," the report said. Most were from the Los Angeles area, and most were either unemployed or students. All were treated during the seven-month period from September, 1965, to last March.

In every case, the victim experienced one or more severe reactions, such as anxiety, depression, or confusion, after the LSD's effects should have worn off. More than half were admitted to the UCLA Neuropsychiatric Institute after receiving emergency treatment. Even in this facility, designed for short-term treatment, most hospitalized patients remained for more than a month.

The authors say that they share general concern over what appears to be a rising number of LSD-related disabilities. The 70 cases treated at UCLA constituted 12 per cent of the Institute's patients during the seven months. Prior to mid-1965, an LSD case there was a rarity, the authors said.

Patient numbers didn't decrease when the new Federal Drug Abuse Control amendments went into effect last February. In fact, March was the clinic's busiest month for LSD cases.

Forty per cent of the patients said they had taken other drugs within six weeks of the time they received treatment for LSD reactions. Thirty-six per cent had histories of chronic marijuana use. On the other hand, another 40 per cent had no history of drug usage. Thirty-seven per cent had received previous psychiatric treatment.

Few of the patients had police records, but a third were unemployed. (It was not determined whether the patients stopped working before or after taking LSD.)

"One former disk jockey said that he had lost his employment after using LSD and had no ambition to start work again," the author said.

A law student said that LSD has opened new vistas to him. "He had 'a perspective of the whole world now' and his legal studies were very dull and uninteresting by comparison," the report said.

The authors noted that none of their patients were "professional-class" persons, in contrast to an earlier report, which said LSD "seems to be mainly used by professionals, intellectuals or other middle-class people."

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## Doctor's Office

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Abraham E. Alpert, M.D., announces the removal of his office for the practice of diagnostic roentgenology to 385 Main Street, West Haven.

Charles A. Bucknan, M.D., announces the opening of an office for the practice of thoracic and cardiovascular surgery and is associated with Dr. Thomas J. Donovan at 85 Jefferson Street, Hartford.

Max Caplan, M.D. and Harvey L. Fritz, M.D., announce the association of Joseph Goodman, M.D., for the practice of internal medicine at 219 West Main Street, Meriden.

Arthur L. Delgrego, M.D., Carl V. Pantaleo, M.D., and Harold D. Batt, M.D., announce the association of Charles M. D'Alessio, M.D., for the practice of diagnostic roentgenology with offices located at 1441 Chapel Street, New Haven, 2447 Whitney Avenue, Hamden and 229 Seymour Avenue, Derby.

Dr. Edward Etkind has become associated with his father, Dr. Meyer Etkind, in the practice of internal medicine at 1546 Chapel Street, New Haven.

Robert F. Jones, M.D., announces the opening of an office for the practice of psychiatry at 546 Williams Street, New London.

James H. Kelleher, M.D., announces the association of William F. McKeon, M.D., in the practice of urology at 55 Broad Street, Norwich.

Dr. Michael J. Lambe announces his association in the practice of general medicine with Dr. Felix G. Sheehan and his brother Dr. Thomas Lambe at 612 Main Street, Middletown.

Gerald Lieberman, M.D., announces the opening of an office for the practice of pediatrics on Whitney Street, Westport.

Stephen L. Lirot, M.D., announces the opening of an office for the treatment of diseases of the eye, ear, nose, and throat at 18 Asylum Street, Hartford.

Joseph P. Macary, M.D., announces the opening of an office for the practice of psychiatry at 49 DeForest Street, Watertown.

Thomas J. McGrath, M.D., announces the opening of an office for the practice of pediatrics and adolescent medicine at 117 Lafayette Street, Norwich.

Donald M. Swanson, M.D., announces the relocation of his office for the practice of medicine to 73 East Main Street, Plainville.

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## Around The State

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### New Haven County

#### BOARD OF GOVERNORS

New Haven County Medical Association

September 29, 1966

The first meeting of the 1966 fall season was held at the Colonial House in Hamden on Thursday, September 29, 1966. It was very well attended and we were honored with the presence of the President of the Connecticut State Medical Society, Dr. Orvan W. Hess.

As is customary at these meetings open discussion of items of the agenda is active and the rule e.g. Medicare and Medicaid Fees; overcharging; the proposed changes in the By-Laws of the Connecticut State Medical Society pertaining to breach of professional conduct which will be a model for all county organizations; changes in our insurance coverage to conform to new principle of coverage by insurance carriers when members are covered by Titles XVIII and XIX; the workshop held recently at the Yale Motor Inn at which Dr. Blasingame, the Executive Vice-President of the A.M.A. made recommendations for strengthening county and state organizations. This is a partial list of the business which was attended to.

This principle has been established in the matter of setting fees (a) "A doctor can charge fees as he wishes provided that he notifies the patient before he undertakes a procedure as to the charges and the patient or his relatives are not under the duress of an emergency; and (b) that he tells the patient that an insurance company might not pay the total bill."

We urge all county organizations to report their Board actions in CONNECTICUT MEDICINE as we have. We like to know what you are doing.

Respectfully submitted,

H. A. LEVIN, M.D., Clerk

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# MEDICAL NEWS

## Infant Deaths Being Reduced

Infant deaths in the U.S. were at a record low last year.

The rate was 24.2 deaths per 1,000 live births, four per cent below the 1963 rate and 17 per cent under the rate in 1950.

The number of infant deaths in 1964 was 98,100, about 5,290 under the previous year, according to provisional statistics of the U. S. Public Health Service.

If this favorable pattern is to continue, however, more mothers and babies must receive proper medical care, says a report by the American Medical Association.

Americans "do not take pregnancy, labor, and delivery seriously enough," says a report by the AMA's Department of Community Health and Health Education and the AMA Committee on Maternal and Child Care. The report appears in the current Journal of the AMA.

"The public must become aware that the highest incidence of death in this country occurs during the perinatal period (before, during and shortly after birth)," the report said.

The report cautioned that comparing infant death statistics with those of other nations with varying types of populations is not a reliable procedure. An earlier report indicated, however, that these crude rates are useful for determining trends within specific geographical and culture boundaries.

"Striking variations in stillbirth and early neonatal (first 28 days after birth) death rates are found from one area to another (within the U. S.) and among social groups within each area," the report said.

"Lower birth weights are associated with certain social differences. Women who work late during pregnancy for example, have babies of lower birth weight than those who do not work during pregnancy or stop work early.

"Death rates are higher among women in the less-favored socioeconomic groups . . . How social factors are translated into biological events is by no means clear, but it is likely that lower birth weights in the less-favored social groups contribute heavily toward higher perinatal mortality rates," the report said.

## New Drug For Gonorrhea

Preliminary tests have been favorable for a new antibiotic used to treat gonorrhea, says a report in the current Journal of the American Medical Association.

The drug, cephaloridine, may prove particularly effective in treating persons allergic to penicillin, which is commonly used against gonorrhea. Cephaloridine may also be effective against gonococcal strains that are showing increasing resistance to penicillin.

The Journal report is from the Communicable Disease Center of the U. S. Public Health Service, Atlanta, and the Fulton County (Atlanta) Health Department.

A cure rate of between 88 and 98 per cent was obtained when 84 male patients were given a single intramuscular injection of the drug. (Doctors aren't sure of the exact cure rate because about half the men didn't return for a checkup. Three who did return had probable reinfections.)

Stressing that this is a preliminary report, the authors point out that larger numbers of patients, including women, now need to be tested. These early results, however, suggest that cephaloridine was effective and produced little, if any, allergic reaction.

Cephaloridine has been produced in England and has been the subject of several favorable clinical reports there, the Journal article said.

Advantages of cephaloridine over a related drug, cephalothin, include a longer level of effectiveness in the blood, greatly increased solubility, and freedom from pain on injection.

"The control of gonorrhea remains a difficult problem in the United States, and estimates place the number of newly acquired cases at over one million yearly," the report said.

"Many reports during the past 10 years have demonstrated an increasing resistance of gonococci to penicillin. This has required that penicillin dosages be increased periodically to maintain satisfactory cure rates.

"While estimates vary widely, it is generally conceded that 5 to 10 per cent of the population is now allergic to penicillin in some manner. Many of these patients receive therapy with alternate and often less effective antibiotics.

"Thus, the search for newer antimicrobial agents useful in the control of gonorrhea becomes increasingly urgent," the report said.

Authors of the report are James B. Lucas, M.D., and James D. Thayer, Ph.D., of the Public Health Service, and Phillip M. Utley, M.D., Terrence E. Billings, M.D., and James E. Hackney, M.D., of the Fulton County Health Department.

### **Ear-Bone Transplants Are Successful**

It may someday be possible to restore hearing by transplanting tiny ear bones from one person to another.

The operation has been successfully performed on cats, and similar research is now underway in human ears, reports a current publication of the American Medical Association.

It's difficult to reconstruct the chain of bones in the "middle ear" of a person with impaired hearing. The task would be easier if a physician could withdraw a bone from a storage bank and implant it in the damaged ear.

This sort of operations was performed on 10 cats by three physicians at the Mayo Clinic and Foundation and the University of Minnesota School of Medicine, Rochester. Their report appears in the current *Archives of Otolaryngology*, published by the AMA.

The anvil-shaped bone of the middle ear, the incus, was removed from cats' ears, and then implanted in other animals. In one case, a bone was successfully re-implanted in the same cat.

The transplants were found to be well tolerated when some were examined five to six months later. New bone had started to grow. This new bone was rapidly replacing transplanted bone by a process the authors called "creeping substitution."

Incus autografts—that is, transplants of middle-ear bones from one ear to another in the same person or animal—have been done several times. These new experiments suggest that transplants may be possible from one person to another. It is their impression, the authors said, that the bones not only grow well, but can function as part of the hearing mechanism.

The authors of the report are David F. Wilson, M.D., Jack L. Pulec, M.D., and Peter D. Van Vliet, M.D.

### **Contact Lenses And Eye Complications**

Fourteen eyes had to be removed or were blinded and 157 eyes were permanently damaged within one year among approximately 50,000 contact-lens wearers, a national survey reports.

The survey, conducted by the American Association of Ophthalmology, is reported in the current *Journal of the American Medical Association*.

There also were 7,607 "reversible ocular changes" among the 49,954 persons examined. These were eye changes from which patients recovered without permanent defects.

"The popularity of contact lenses has exceeded the public knowledge of potential hazards associated with their use," said the Committee on Contact Lenses of the AAO.

The report listed precautions for contact-lens wearing, and suggested responsibilities of ophthalmologists in fitting the lenses. It made no recommendations, however, concerning the relative merits of the various kinds of contact lenses or conventional glasses.

Eye complications associated with contact lenses are more frequent among older persons and those with previous eye injuries or disease, the report said. Complications also are associated with prolonged wearing or with sleeping with the lenses on the cornea. Eye problems are made more severe by wearing the lenses after the complications appear, the report said.

The survey consisted of questionnaires mailed to 8,181 ophthalmologists. A total of 1,904 returned answers concerning 49,954 patients seen in the 12 months prior to April, 1960.

Infection was present in each of the 14 reported cases of eye loss or blindness. In four cases, the infection was due to fungi. In 10 cases, it was bacterial or due to unidentified organisms.

The report pointed out, however, that wearing contact lenses with proper technique on the normal eye does not alter the eye's normal bacterial flora.

Six of the 14 patients required removal of the eye. Two required corneal-graft operations; only one of these recovered vision in the eye, and it was reduced to 20/50.

The only incident of blindness in both eyes caused by contact lenses was reported previously in 1956, and was not included in this report.

### **Alcoholism Recognized As A Disease**

Recent court decisions recognizing that alcoholism is a disease, not a crime, are in agreement with a position adopted by the American Medical Association ten years ago and reaffirmed in 1962, says an editorial in the current *Journal of the American Medical Association*.

As a result of the court decisions, the medical profession faces increasing responsibility for "a wide range of alcoholic problems previously left primarily to law enforcement agencies," said the *Journal* editorial.





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# angina of anger

**“My life is in the hands of any rascal who chooses to annoy and tease me.”<sup>1</sup>** So said the great British surgeon and anatomist, John Hunter, realizing that he could not control the anger which precipitated frequent and severe attacks of angina pectoris. According to Mettler: “His statement was no exaggeration. On October 16, 1793, he attended a meeting of the St. George’s hospital staff, and, while defending the interests of several students, he was contradicted and thoroughly antagonized. The pains of angina commenced, he started toward another room, gained it, and fell dying into the arms of a physician.”<sup>2</sup>

**Why Edward Jenner withheld his paper on angina** In 1777, at an earlier stage of the condition, Hunter’s angina alarmed a favorite pupil, Edward Jenner, who wrote to Dr. Heberden that he feared his teacher was “affected with symptoms of the Angina Pectoris.”<sup>3</sup> So concerned was Jenner about his former teacher’s emotion-related condition that he deliberately cancelled publication of a paper on angina pectoris, fearing that

Hunter would read it, and have “his fears excited by its truly formidable nature.”<sup>4</sup>

**Severity of angina described** Hunter’s brother-in-law, Dr. Everard Home, who witnessed his death and performed an autopsy, gave this account of the later stages of the condition:

“... the pain became excruciating at the apex of the heart; the throat was so sore as not to allow of an attempt to swallow anything and the left arm could not bear to be touched....

“The affections above described were, in the beginning, readily brought on by exercise... but they at last seized him when lying in bed, and in his sleep....”<sup>5</sup>



**18th century ancestor of the modern coronary candidate** Surgeon, anatomist, pathologist, physiologist, geologist, and teacher, Hunter had a passion for research which led him to disregard his practice, his health and even the



When the Irish giant O'Brien learned that Hunter desired his skeleton for a museum, he willed that his body be sunk at sea in a lead coffin. But Hunter was not to be denied. According to Major, he bribed the watchers and finally obtained the body at a cost of 500 pounds although he had to borrow money to pay the men."<sup>3</sup> In 1767, he experimentally inoculated himself with gonorrhea and syphilis, treated himself with mercury for three years, and was apparently cured.<sup>5</sup> Hunter had feelings of inadequacy about his education and speaking ability, but this did not prevent him from engaging in hard driving and abrupt behavior with his colleagues. His competitiveness with his physician older brother was also well known, and resulted in complete estrangement between the two men.<sup>2,3</sup> Today, the personality traits seen in John Hunter are recognized to be important predisposing factors in the development of coronary artery disease—often manifested as angina pectoris. According to Friedman and Rosenman,<sup>6</sup> in a group of men whose behavior was characterized by intense competition and competitive drive, the greater than average incidence of angina pectoris was among those in normal conditions noted.

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**Actions:** The exact cause of angina pectoris (that is, the pain associated with coronary artery disease) remains obscure, despite the numerous and often conflicting hypotheses concerning its pathophysiology. Therapy at the present time, therefore, remains essentially empiric. Customarily, clinical improvement has been measured by: reduction in (1) number, intensity and duration of angina pectoris attacks and (2) necessity for glyceryl trinitrate intake for prevention or relief of anginal attacks.

Peritrate SA Sustained Action (pentaerythritol tetranitrate) 80 mg. has been reported in clinical usage to reduce in number and severity the incidence of angina pectoris attacks, with concomitant reduction in glyceryl trinitrate intake.

In the evaluation of Peritrate (pentaerythritol tetranitrate) and Peritrate SA Sustained Action (pentaerythritol tetranitrate) 80 mg. in angina pectoris, clinical improvement has been customarily measured subjectively by reduction in number and severity of attacks and necessity for glyceryl trinitrate intake for prevention or abortion of anginal attacks. Individual patterns of angina pectoris differ widely as does the symptomatic response to anti-anginal agents such as pentaerythritol tetranitrate. The published literature contains both favorable and unfavorable clinical reports. In conjunction with total management of the patient with angina pectoris, Peritrate (pentaerythritol tetranitrate) and Peritrate SA Sustained Action (pentaerythritol tetranitrate) 80 mg. have been accepted as safe for prolonged administration and widely regarded as useful.

**Animal pharmacology:** In a series of carefully designed studies in pigs, Peritrate (pentaerythritol tetranitrate) was administered for 48 hours before an artificially induced occlusion of a major artery and for seven days thereafter. The pigs were sacrificed at various intervals for periods up to six weeks. The result showed a significantly larger number of survivors in the drug-treated group. Damage to myocardial tissue in the drug-treated survivors was less extensive than in the untreated group. Pigs rather than dogs were used because their coronary artery distribution more closely resembles that of human beings. Studies in dogs subject to oligemic shock through progressive bleeding have demonstrated that Peritrate (pentaerythritol tetranitrate) is vasoactive at the post-arteriolar level, producing increased blood flow and better tissue perfusion. These animal experiments cannot be translated to human behavior.

**Indications:** Peritrate SA Sustained Action (pentaerythritol tetranitrate) 80 mg. is indicated for the relief of angina pectoris (pain associated with coronary artery disease). It is not intended to abort the acute anginal episode but is widely regarded as useful in the prophylactic treatment of angina pectoris.

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**Warning:** Data supporting the use of Peritrate (pentaerythritol tetranitrate) during the early days of the acute phase of myocardial infarction (the period during which clinical and laboratory findings are unstable) are insufficient to establish safety.

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The statement was approved by the AMA's Committee on Alcoholism and Addiction and the AMA Council on Mental Health.

The most immediate task, the editorial said, is to develop guidelines for diagnosing alcoholism "which are as clear and precise as possible and which satisfy both medical and legal definitions."

A second obligation of the medical profession is to "foster the admission of alcoholics to those general hospitals that do not now admit such patients" and to establish detoxification units closely affiliated with established, long-term treatment centers and associated agencies.

"Next, we (physicians) should play an important role, not only in the education of many members of our own profession, but also in educating police and other concerned groups about issues of acute and chronic alcoholic infirmities."

Finally, physicians should integrate their specialized skills on an equal basis with other professions "in those long-term endeavors (of alcoholic management) in which purely psychiatric or other medical factors are not predominant," the statement said.

In two recent decisions, courts in North Carolina and the District of Columbia recognized alcoholism as a disease, and defined frequent public appearance in an intoxicated state as a symptom of alcoholism, not a criminal offense.

The decisions in the Driver case in the Fourth Circuit Court in North Carolina and the Easter case in the Circuit Court for the District of Columbia are "important landmarks," the Journal editorial said.

"These decisions do not negate statutes punishing ordinary public drunkenness; neither do they deal with the . . . culpability of persons carrying out unlawful and antisocial acts while under the influence of alcohol.

"They do portend, however, the end of the time-worn practice of meeting the problems of public drunkenness . . . of chronic alcoholic persons primarily by incarcerating them as criminals," the editorial said.

The extent to which physicians assist the alcoholic in obtaining proper medical care and other help "will be a measure of our response to the challenge implicit in these decisions," said the editorial.

## **Sports And Bone-Joint Injuries**

There is some risk that the 9- to 14-year-old who competes in sports may injure his growing bones in ways that may hamper growth or result in deformity.

The dangers have been exaggerated, however; the advantages of sports for youngsters far outweigh the disadvantages, say an article and editorial in the current Journal of the American Medical Association.

The potentially crippling injury that causes great concern is damage to the epiphyses, the pieces of bone joined by cartilage to the body's long bones. Growth takes place in these cartilaginous joint areas during childhood. Eventually, the bones grow together.

If the epiphyseal joint is damaged, it may stop growing, or grow in a way that leads to deformity. Prompt recognition and treatment of these injuries, however, greatly reduces this possibility, say the Journal article's authors, Robert L. Larson, M.D., and Robert O. McMahan, M.D., of Sacred Heart Hospital, Eugene, Ore.

The authors do suggest that certain types of youngsters should postpone sports activity until they develop further. Most susceptible to epiphyseal injury are obese children and tall, uncoordinated, lanky youngsters with poor muscle development.

Reviewing 1,338 athletic injuries treated by four physicians (all orthopedists) in the Eugene area, the author found that 20 per cent of those injured were 14 or younger. Only six per cent of this group's injuries involved the epiphyses, however, and growth disturbances were "the exception rather than the rule," in these injuries.

Some activities are unusually hazardous for young athletes, the authors said. The base-runner's slide in baseball is a cause of frequent bone and joint injury. Consideration is being given to eliminating slides from Little League play.

One medical study suggests that curve balls should be ruled out for 9- to 14-year-old pitchers, and that they be limited to two innings of play per week. Little Leagues already limit pitchers to four to six innings, the authors said.

Youngsters in the 12- to 15-year-old group are frequently injured after landing stiff-legged during basketball rebounding, pole vaulting, and high jumping.

The authors said attention should be given to so-called "sprains" on weight-bearing joints. These may be symptoms of damage to epiphyseal areas.

"There undoubtedly has been an excess of speculation and condemnation surrounding competitive athletics among adolescents, when there should have been more consideration for ways to

# Connecticut Medicine

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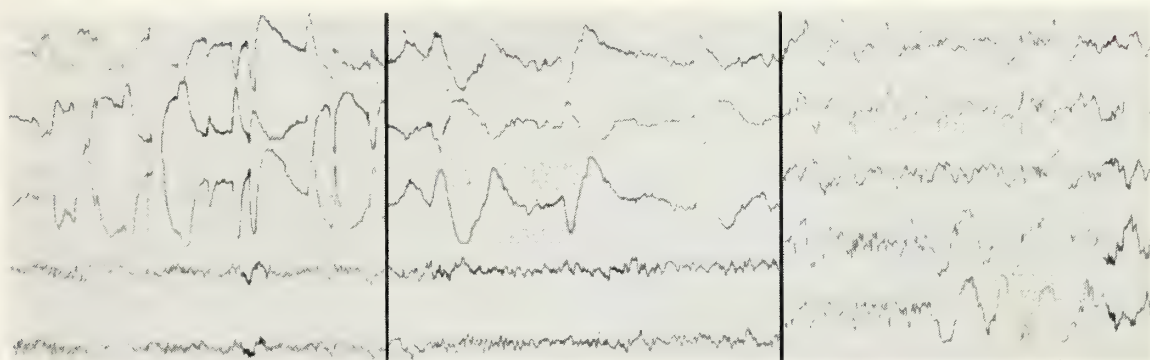


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Connecticut State  
Medical Journal

Volume 30 / December 1966 / Number 12

## SLEEP—FROM ALPHA TO DELTA



ALPHA

REM

DELTA

"Sleep—From Alpha to Delta," By Gay Gaer Luce and Julius Segal, April 17, 1966

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## editorials

### Thymoma And Immunologic Deficiency

One mechanism of immunity is thought to be the lymphocyte which gives rise to gammaglobulin. The cells are generated in the thymus migrate into the blood stream and lymph to populate independent centers in the spleen, lymph nodes, Peyer's patches in the gastrointestinal tract and other lymphoid tissue. Here under antigenic stimulation, the lymphocyte becomes immunologically competent.<sup>1</sup> If the thymus is removed before the immune apparatus is developed such animals show a poor development of peripheral lymphoid structures and marked disturbances of immune functions of the body.

Much evidence exists especially derived from experiments involving immunosuppression with irradiation and drugs that the small lymphoid cells do participate in the early phases of antibody production.<sup>2-7,9</sup> In adult life the thymus seems to sustain the lymphoid systems both under conditions of extreme depletion as by heavy irradiation, as well as under conditions of normal wear and tear.

Once the peripheral lymphoid structures are populated by lymphocytes of thymic origin, then the immunoglobulin producing system and probably its maintenance can be controlled by these peripheral lymphoid centers. Gabrielson believes that the Peyer's patch type of tissue in the gastrointestinal tract in mammals, is the mammalian equivalent of the bursa of Fabricius which clearly controls the development of the immunoglobulin production system in chickens. However, there still remains the question of what makes lymph-

ocyte proliferate to offset the process of wear and tear.

Certain clinical diseases are associated with failure to produce immunoglobulin.<sup>11</sup> In one there is extreme lymphopenia, failure of development of peripheral lymphoid tissue agammaglobulinemia and understandably extreme susceptibility to a variety of infections. This type may be a result of inherited traits. Although their thymic tissue is normal all the remainder of the lymphoid system is atrophic, small, abnormal in structure and poor in lymphoid cells. It occurs only in boys and they are very susceptible to bacterial infections. There is an absence of plasma cells as well and failure of plasma cell response to the most intense antigenic stimulation. Since the thymus appears normal such patients act as if something is inhibiting lymphocyte proliferation.

A second clinical association of the thymus with failure of immunoglobulin production is found in certain thymomas.<sup>10</sup> The first such patient described by Gabrielson in 1953 had acquired agammaglobulinemia. In such patients the gammaglobulin level may fall well below 400 mg/100 m.l. and even as low as 100 mg/m.l. The typical age of such patients, of whom there are now 20 described, is 40 years of age. There has been instances of clinical immunologic deficiency developing years after thymomas were diagnosed by X-ray. In such patients the failure of the immunoglobulin producing system could be occurring over a prolonged period and only reach troublesome levels perhaps in the range of 400 mg of gammaglobulin/100 m.l. after an extended period. Many are not extreme although some as in Gabrielson's case are.

#### THE COVER

**ALPHA**—The subject drowzes, on the edge of sleep. Top three EEG channels show rolling movements of right eye, left eye and both. Two bottom tracks trace brain's electrical changes, here the even pattern of alpha rhythm, indicating relaxation.

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**DELTA**—Marked by large, slow brain waves (two bottom channels), this is the deepest stage of sleep, the first to be made up for after total deprivation. Though its restorative function is essential, it is also a period of somnambulism and nameless terrors.

The association between thymoma and immunologic deficiency has up to the present time received no ready explanation. The important discovery by White and his group of the existence of two thymic hormones is the first ray of light that promises to bring some explanation into the bewildering array of disorders now known to be associated with the thymus.<sup>9</sup> One such hormone, thymosin causes lymphocyte proliferation. Its absence would stop lymphocyte growth and the production of natural and acquired immunity that comes from lymphocyte proliferation.

Another hormone as yet unnamed by White and his group causes inhibition of lymphocyte proliferation. Such hormone if underproduced would throw the balance in favor of lymphocyte overproduction, and increased natural and acquired immunity. If, however, the inhibitory hormone is overproduced by a thymoma or other as yet unknown factors, it would cause disappearance of the lymphocyte and its product immunoglobulin. This could then give rise to agammaglobulinemia and all its dire consequences.

With the illumination into this complex field that must come from the discovery of thymic hormones, we are brought onto the threshold of additional insights into the understanding of the function of the thymus and the cell system dependent on it.

L.H.N.

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## The Artificial Heart

There has been widespread interest in reports of "artificial hearts" which have been inserted in patients in two centers in the United States. The lay press has provided widespread coverage of these procedures and it is necessary for the physician to understand the present status of this therapy as well as the advances which can be confidently expected in the near future.

Since the recent introduction of coronary units in our larger hospitals we have gained a better understanding of the exact cause of death following acute myocardial infarction. A slight improvement in mortality statistics has been achieved by early recognition and effective treatment of disorders of cardiac rhythm. We also have a better understanding of the nature of cardiogenic shock and its management.

However, when the heart fails as a pump the most logical way of aiding the patient is to provide a temporary auxiliary pump. The present mortality from myocardial infarction will be significantly lowered only when such mechanical assistance for the circulation will be available from suitable personnel and suitable equipment. Of course heart-lung machines which can safely take over the entire function of the heart and lungs for periods up to four hours are now in routine use for heart surgery. However, the routine use of such equipment in a patient with acute myocardial infarction is impractical, first because a thoracotomy is required and second because the longer perfusions such patients require would damage the formed elements of the blood and the protein and lipid elements of the plasma.

We must recall that the greater proportion of this damage occurs in the oxygenator not in the relatively simple and atraumatic pumps. Furthermore the patient in acute coronary shock or acute pulmonary edema does not need an oxygenator. He needs only a more effective pump.

Several papers in a recent issue of the *Canadian Medical Association Journal*<sup>1</sup> describe the various modalities that are now available for the provision of temporary circulatory support in the acutely ill patient. One paper by Soroff describes the use of a permanently implanted subcutaneous ventricle,



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**\* Reference:** Litchfield, H. R.: Archives of Pediatrics,  
71:367-369, Nov. 1954

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but the main emphasis in the other papers is on the provision of temporary treatment in an emergency situation.

In this context we need to remember that the "booster hearts" which have received such widespread press coverage are not hearts at all but a modified version of left-ventricular by-pass and synchronous arterial assistance which require major not minor surgery and are designed for use over a period of days and weeks. The technique became possible only after the development of plastic membranes in which heparin is chemically bonded to the surface and this allows such units to be inserted without fear of subsequent thrombotic phenomena.

Left ventricular by-pass has an advantage of not requiring an oxygenator and can be performed either with a trans-venous, trans-septal cannula without a thoracotomy or else with direct cannulation of the appropriate chamber after a thoracotomy. The closed chest approach has the virtue of requiring only local anesthesia, but it has the difficulty and dangers of passing a large cannula into a very specific site in a very ill patient. On the other hand open chest left ventricular by-pass requires a major surgical procedure not well suited for an acutely ill patient.

The device implanted by the Houston group is a more permanent form of left ventricular by-pass in which the blood is removed from the left atrium and pumped by an auxiliary "ventricle" into the thoracic aorta. The assisting ventricle is placed in the left pleural cavity and is activated by compressed air which reaches it via a transthoracic tube.

Synchronous arterial assistance is a technic whereby an auxiliary ventricle accepts arterial blood during ventricular systole and returns it to the arteries during diastole, then an oxygenating device is not needed. This type of circulatory assistance greatly reduces the oxygen needs of the left ventricular myocardium. There is required fine electronic monitoring which synchronizes the stroke of the pump with the heart of the patient.

When the form of mechanical assistance is applied via a femoral artery cannula the pulse waves from the patient's left ventricle and from the assisting pump meet in the aorta near the renal artery and lead to changes in the vascular resistance of various parts of the body.

In Kantrowitz's device<sup>2</sup> the augmenting ventricle is inserted in the chest. Blood is taken into the pumping chambers from the ascending aorta during systole and then pumped into the thoracic aorta during diastole. The augmenting ventricle is activated pneumatically via a transthoracic tube.

In veno-arterial by-pass with oxygenation, blood is removed through a large cannula inserted into the femoral vein, oxygenated in a small disposable oxygenator and returned to the body via the femoral artery. The surgical procedure is small, performed under local anesthesia, and approximately half the cardiac output can be pumped by the assisting ventricle. However, the technic is only suitable for temporary assistance over a period of perhaps four to eight hours.

In short there are at present two areas of mechanical circulation assistance under development. Those procedures designed for use in the urgent situation of the patient in coronary shock or acute heart failure following acute myocardial infarction. Then there are the more permanent forms of assistance which involve modifications of this equipment to allow semi-permanent extra-corporeal placement of a prosthetic pump.

When we glance at the specialized equipment, personnel and materials required for successful mechanical assistance for the circulation we get a glimpse of the direction medical progress is taking towards teams of specialists not just physicians and surgeons but engineers and others and away from the individual physician. In gaining one asset let us strive not to lose an equally valuable one, the personal physician.

L.H.N.

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## Curing The Water Pollution Problem

Over 100 years ago Parliament couldn't meet because of the stench from the Thames River caused by sewage discharged into it from growing London.<sup>1,2</sup> How did they solve this nuisance; by extending the pipes to discharge the waste into

the river far downstream. The lawmakers did not understand the role of water in the transmission of disease nor did they consider longer range solutions. It was the immediate unpleasantness that they eliminated by this short range solution. The problem was transferred to the downstream communities.

Once bacteriology was developed, the role of water in the transmission of typhoid and other enteric bacterial diseases was clarified and the introduction of water filtration processes greatly reduced bacterial concentration. Those towns which then still used unfiltered water like Pittsburg and Cincinnati had three times as many deaths from typhoid as others who used filtered water.

In the next phase water treatment plants were introduced by those towns and cities using rivers as sources of water. The treatment was aided greatly by the introduction of chlorine for water disinfection. This seemed to make possible production of bacteriologically safe water at very little cost even when raw water of very poor quality was being treated. At this time water-borne viral infections were not considered. Neither was the problem of chemical pollutants which has loomed large with the increase of industrial wastes being discharged into rivers and lakes. Because bacterial threats to the water users were greatly reduced by filtration and water treatment, the pressure for water pollution control was also reduced.

As outbreaks of water borne disease have become relatively rare, we are becoming increasingly concerned about water borne viral diseases especially infectious hepatitis. In this country as contrasted with New Delhi, water seems not to be a major factor in transmission of the disease. It may however be a factor in introducing the disease in a community. If this is so then in the treatment of water subject to sewage pollution, disinfection be carried out beyond that needed to insure compliance with current bacteriologic quality standards.<sup>3,4,5</sup>

The possible effects on health of a variety of unidentified chemical compounds that enter water supply sources with sewage and industrial waste needs much more knowledge. Our water treatment plants do not remove most dissolved solids. They only remove particulate matter including bacteria and colored organic compounds arising from leaching of vegetation. Accordingly we cannot depend on the ability of water treatment plants to cope with steadily increasing chemical pollution as water reuse increases. Two outbreaks of water-borne gastroenteritis occurred in communities on the Kana-wha and Ohio rivers after a sudden rise in water levels and also in the Ruhr Valley in Germany.<sup>3</sup> In

both bacterial content of treated water was good but heavy chemical pollution was noted.

The concern over increasing chemical pollution is enhanced by the possible effects of chronic exposure to a wide variety of substances that are finding their way into water containing municipal and industrial wastes.<sup>3</sup> We need much more knowledge of the possible physical effects of these materials to ensure that hazardous substances are removed by water treatment and at the source. Pollution then does preclude the use of certain waters as sources of water supply or for recreation. It places an economic burden on water users in increased treatment costs and it helps to create an environment that is less enjoyable and hence less healthful than it might otherwise be.<sup>4,5</sup>

Water pollution obviously exists because to prevent it means an economic burden. However Woodward points out that at present this burden of cleaning up streams, lakes and coastal waters is three dollars per person per year. But this will grow because of rapid urbanization and population growth. By 1980 the cost may rise to about \$10 per capita per year, a trivial item of expense in most personal budgets nor a serious drain on the national economy. This is obvious when comparing this with certain other costs. The Vietnam War costing twenty-four billion dollars a year is a tax of \$120. per capita per year. The total war budget is 62 billion dollars per year or \$300. per capita. The space projects, another war effort is five billion dollars per year or \$25. per capita. So is the Atomic Energy Commission of five billion per year. The foreign aid programs have averaged four billion per year or \$20. per capita. To have difficulty to raise three or even ten dollars per capita for clean water seems to say the least indifference to the public welfare.

Besides indifference another of the features of the water pollution problem that has deterred attack on it is the fact that the damages caused go beyond the community or industry giving rise to it. The waste is discharged downstream to affect other communities, the same method Parliament used in 1858. There is then no economic incentive to the waste producers to eliminate the pollution.

Woodward mentions several possible approaches to this problem, such as charging the waste producers for the damages caused by the waste discharge. This of course does not enthruse the industries concerned nor the politicians who would prefer to transfer the cost to the tax-payer. As far as abating pollution due to municipal wastes, Federal and State grant-in-aids to communities certainly would accelerate progress.<sup>5</sup>





## Breast-feeding and the “modern mother”

Despite a mild resurgence of interest in the importance of breast-feeding a few years ago, many women today do not choose to nurse their young. This is for a variety of reasons—social, economic, cultural and sometimes medical. In such cases the physician's task is to find the most suitable means of preventing lactation and easing the pain of breast engorgement.

### The means of therapy

The value of hormone therapy for this indication is of course well established. Both androgen and estrogen are known to inhibit the production and secretion of the lactogenic hormone by the anterior pituitary. As estrogen levels decline sharply at parturition, lactogenesis is established. When androgen and estrogen are administered to the patient before the release of the lactogenic hormone lactation and breast engorgement are usually prevented.

### The time of therapy

The time of administration of this combined medication is crucial; it must be given early enough to suppress the pituitary prolactin and last long enough to permit physiologic readjustment during the puerperium. Excellent results are most often seen when therapy is administered before the onset of the second stage of labor.

However, factors other than effectiveness must also be considered. The agent selected should not interfere in any way with parturition, subsequent uterine involution and the restoration of normal ovarian cyclic function. Furthermore, it should not cause rebound breast engorgement or other manifestations of hormonal imbalance.

### A balanced formulation

Providing single-dose therapy for the prevention of lactation and breast engorgement, Deladumone OB is a potent androgen-estrogen combination with a prolonged action. The optimal balance of androgenic and estrogenic hormones achieved in this preparation minimizes the disadvantages inherent in single hormone therapy, such as rebound breast engorgement. Involution of the uterus and resumption of menstrual cycles are not affected.

As reported in a recent published study (Roser, D. M.: *Obstet. & Gynec.* 27:73, 1966), Deladumone OB provided good suppression of breast engorgement in 95.3% and suppression of lactation in 81.1% of 86 obstetrical patients. These results are in general agreement with those of many earlier investigations; in several studies this injectable androgen-estrogen combination proved to be superior to oral medication.

### Dosage:

As a single injection of 2 cc. before the onset of the second stage of labor.

### Contraindications:

Established or suspected mammary cancer or genital malignancy.

### Precautions and Side Effects:

Certain patients may be unusually responsive to either estrogenic or androgenic therapy. In such individuals virilization, uterine bleeding or mastodynia may occur.

### Supply:

Deladumone OB, providing 180 mg. testosterone enanthate and 8 mg. estradiol valerate per cc., is available in 2 cc. Unimatic® disposable syringes and in 2 cc. vials. Both preparations are dissolved in sesame oil, with 2% benzyl alcohol as a preservative. *Before use, consult product literature for full prescribing information.*

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As our awareness of the water pollution problem grows and its dire consequences to health and recreation becomes more clear, we begin to realize, how urgent it is to improve the techniques now available for dealing effectively with them. Suitable solutions are not in sight for the problem of acid-mine drainage which damages many of the streams in the coal-mining area of the Appalachian highlands. How to prevent the factors which threatens the beauty and utility of many lakes is not well enough understood to enable planners to devise optional schemes for dealing with them. Some lakes like Tahoe can be saved by diversion of all wastes out of the drainage basin, a method scarcely feasible for large lakes like Erie. Then is the problem of reducing phosphate input into lakes; a problem not yet solved especially since we do not yet know the critical permissible levels of phosphate in water not to speak of the costs involved.<sup>6</sup>

Another problem arises from the fact that most older cities have combined sewers that carry both sanitary sewage and storm water. During rain storms these sewers discharge storm water plus wastes to water courses. This is a serious problem for the Charles river in metropolitan Boston. It is also a serious problem in many of the great lakes and coastal cities where overflows pollute bathing areas.

Above all there is need for better knowledge of the effects of water pollutants on human beings and various forms of aquatic life. How clean should water be? How successful are our bacteriologic standards for bathing waters? How effective are our water treatment standards in eliminating viral diseases in water users? What are the effects on human beings of various chemical pollutants? What is our knowledge about the quality requirements of aquatic life? Without such answers how can we set realistic goals for water pollution abatement?

At present there is also a serious shortage of scientific and technical personnel to conduct the needed research and development work, to administer federal and state programs and to design and operate the necessary facilities. As these problems are solved it should be possible to meet all the public expectations for effective action against water pollution.

L.H.N,

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The Complexity Of The Shock Problem

In physiologic terms the syndrome of shock includes a number of widely different conditions which share only the finding of hypotension. The causative mechanisms in these different forms of shock may be so varied that no one mode of therapy can be applied to all. An example of this problem can be seen when one contrasts the treatment in hypovolemic and cardiogenic shock. Both showed hypotension, oliguria, cold sweaty extremities and all the biochemical and clinical features which are accepted as constituting the syndrome of shock. However while fluid administration is vital in hypovolemic shock it could be fatal in cardiogenic shock. Consequently before any treatment of shock is instituted, we need to know whether it is hypovolemic, cardiogenic or septic.

If there had been hemorrhage, recent fluid loss from vomiting, diarrhea, nasogastric aspiration, or trauma including extensive operative procedures the patient is probably suffering from hypovolemic shock. Simple bedside observations reveal that in hemorrhage there is pallor and restlessness, in dehydration dull apathy. In all forms of hypovolemic shock there is collapse of the normally visible veins in the extremities where there is intense vasoconstriction. The skin becomes mottled blue-white, sweaty and cold. The failure of venous return causes a sharp drop in central venous pressure.

Cardiogenic shock is strongly suggested by the typical chest pain, electro-cardiographic findings and serum enzyme changes. In such a patient the central venous pressure will probably be raised initially, and will rise rapidly with the infusion of only small amounts of fluid.

A septic origin of shock may be suggested by chills, fever, intra-abdominal symptoms or recent genito urinary manipulation. In this form of shock there occurs vasodilatation in the periphery and we find warm dry skin and a wide pulse pressure.

In advanced shock intense vasoconstriction greatly limits the reservoirs capacity of the venous systems. Under these circumstances small amounts of fluid will cause a rise in central venous pressure even in hypovolemic patients. It is this form of intense vasoconstriction that can be "broken" by the use of vasodilator agents.

We could have a good guide in the treatment of any form of shock if we had repeated recordings of arterial blood pressure, central venous pressure and hourly urine output. Only in this way can the guidelines be established and the necessary moment to moment adjustments in therapy carried out. The central venous pressure measurements cannot be made through the usual i.v. needle in the forearm vein, but by passing the catheter up the brachial or the cephalic vein to reach the outlet. When the tip of the catheter is in proper position there is free fluctuation of the fluid column in the tube coincident with respiration.

In shock resulting from fluid loss the central venous pressure will begin to rise only after large amounts of fluid have been given. By this time a clinical response is shown by improvement in blood pressure, and urine output is generally evident. This point needs emphasis because the use of vasodilator agents in the presence of hypovolemia could be serious. All the elements of hypovolemic shock respond rapidly to volume replacement by blood, ringer lactate and a dextran. The labored breathing becomes easier and the heart rate slows. The provision of adequate fluid volume is the best vasodilator treatment available in early hypovolemic shock.

In advanced shock intense vasoconstriction greatly limits the reservoirs capacity of the venous system, produces hypoxia and anoxia of tissues. If allowed to go on it can cause necrosis of the gastrointestinal mucosa. In this form the vasoconstriction can be "broken" by the use of vasodilator agents. If treatment is started before there is diffuse cell damage, the cardiac output, renal blood flow, and urine output will improve and heart function will also improve.

There are a number of different vasodilator drugs acting at different levels in the sympathetic nervous system. Some like tetraethylammonium interrupt the tonic vasoconstrictor discharge in the sympathetic outflow. These agents however do not interfere with the action of vasoconstrictors in the small blood vessels. Ganglionic blocking drugs have been used during surgical therapy to diminish bleeding and lessen the strain on the left ventricle when the aorta is clamped in the chest, and more recently to reduce the blood loss in hemorrhagic shock caused by bleeding peptic ulcer.

Another group of drugs such as Dibenzylene block the alpha receptors in vascular smooth muscle rendering them refractory to vasoconstriction by catecholamines. They also reduce the vasoactivity of such agents as histamine and serotonin. The effect of phenoxybenzamine (Dibenzylene) is quite dramatic in reversing epinephrine effects. The small vessels previously so constricted that blood flow ceased, open and enlarge to a size greater than normal. Flow increases, veins dilate, red cells within the vessels are more saturated with oxygen.

When Dibenzylene is used in shock a similar picture is seen. The sweaty cold extremities become warm and dry and pink. The previously narrow thready pulse becomes full and readily palpable, the venous pressure which previously may have been raised by vasoconstriction falls. The veins on the dorsum of the hands and feet now become visible. However because Dibenzylene produces a rapid increase in the capacity of the venous system, it is imperative that at the same time as it is being administered that additional amounts of fluid be provided rapidly to fill the enlarged vascular space, otherwise the blood pressure will drop rapidly below the levels needed to perfuse the heart and brain.

Accordingly Dibenzylene is given slowly in a dose of 1 mg/kg in 200 m.l. of 5 percent of glucose over approximately one minute by i.v. drop with repeated measurement of central venous and arterial pressure. Fluids either blood or lactate are needed continuously to maintain a positive venous pressure. A sudden drop in blood pressure now requires that Dibenzylene be discontinued and fluid added rapidly until the arterial pressure is restored to an adequate level.

There are additional thoughts to be borne in mind in dealing with a patient in shock. The lungs may be filled with secretions, requiring endotracheal suction especially at the onset of shock when patients should be turned frequently from side to side and urged to cough. Reduced sodium ions can be associated with reductions of plasma and extra cellular fluid volume thereby increasing the toxicity of Potassium. A calcium deficit may be involved if much citrated blood is used requiring adding 1 gram of calcium gluconate for 5 units.

Vasoconstrictive agents in the presence of adequate blood volume, early in the course of treatment may improve coronary blood flow. However, later when secondary vasomotor substances may be circulating in the blood, addition of vasopressor materials will be of little avail and may do harm.

Isoproterenol (isuprel) is increasing in prominence as a potent agent in shock and may well be of value early in the shock state. Its stimulating prop-



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effects are encountered, the drug should be discontinued and appropriate measures taken. Use on infected areas should be attended with caution and observation, bearing in mind the potential spreading of infection and the advisability of discontinuing therapy and/or initiating antibacterial measures. Generalized dermatological conditions may require systemic corticosteroid therapy. Steroid therapy, although responsible for remissions of dermatoses, especially of allergic origin cannot be expected to prevent recurrence. The use over extensive body areas, with or without occlusive nonpermeable dressings, may result in systemic absorption. Appropriate precautions should be taken. When occlusive nonpermeable dressings are used, miliaria, folliculitis and pyoderma will sometimes develop. Localized atrophy and striae have been reported with the use of steroids by the occlusive technique. When occlusive nonpermeable dressings are used, the physician should be aware of the hazards of suffocation and flammability. The safety of use on pregnant patients has not been firmly established. Thus, do not use in large amounts or for long periods of time on pregnant patients.

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**This clinical study shows** that the two combinations of antibiotics were not superior to some of their single components. The authors point out that antibiotic antagonism often negates theoretical advantages of multiple therapy. Coly-Mycin Injectable (colistimethate sodium) was one of the single components that was shown to be equal to the combinations and eradicated bacteriuria in two-thirds of the patients.

Theoretical choice of multiple antibacterial therapy has been shown to be no more effective than one well-chosen agent which also offers least patient exposure to possible side reactions, toxicities, allergic manifestations and higher drug costs.

1. McCabe, W. R., and Jackson, G. G.: New England J. Med. 272:1037, 1965.



in gram-negative urinary tract infections often the single well-chosen agent



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**Adverse Reactions:** Occasional reactions such as circumoral paresthesias, tingling of the extremities, pruritus, vertigo or dizziness may occur. Reduction of dosage may alleviate symptoms. Therapy need not be discontinued, but such patients should be observed with extra care.

**Warning:** Patients should be cautioned not to drive vehicles or use hazardous machinery while on therapy.

**Precautions:** In cases of impaired or suspected renal impairment, use with greater caution and reduce dosage in proportion to extent of impairment. Transient elevations of BUN have been reported. As a routine precaution, appropriate blood studies should, therefore, be made during prolonged therapy.

As with all polypeptides, the possibility of muscular weakness, including apnea, due to inadvertent overdosage or normal dosage in the presence of impaired renal function, should not be overlooked. In cases of apnea, medication should be promptly discontinued and assisted respiration given until serum levels fall and normal breathing is restored.

Other antibiotics, such as kanamycin, streptomycin, dihydrostreptomycin, polymyxin, and neomycin, may also have varying neurotoxic or nephrotoxic potential. They should be used with great caution concomitantly with Coly-Mycin Injectable (colistimethate sodium).

**For deep intramuscular injection only.**

**Dosage:** By the I.M. route only, in 2 to 4 divided doses ranging from 1.5 to 5 mg./Kg./day (0.7 mg. to 2.3 mg./lb./day). Average adult dose is 2.5 mg./Kg./day (1.1 mg./lb./day). In the presence of bacteremia, septicemia, or other serious infection, greater than average doses may be required; however, maximum daily doses should not exceed 5 mg./Kg. (2.3 mg./lb.) where renal function is normal.

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erties on the myocardium and bronchodilator and peripheral vasodilating properties could be useful.

Finally we must recognize that vasodilator agents are not useful in septic shock where there is already evidence of vasodilatation.

One final thought is the need of using hypothermia to reduce the temperature to normal of patients with hyperthermia. This will reduce metabolism, oxygen used and preserve tissues long enough to combat shock and its consequences.

This short survey reveals both the complexity of problems in shock therapy and a clearer understanding of how to deal with the various states of shock.

L.H.N.

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## Inflammation, Kinins And Cortisol

Kinins are naturally occurring polypeptides of known structure whose pharmacologic effects resemble the manifestations of acute inflammation. In extraordinarily minute quantities 0.1 to 1 milligram per ml. they produce vasodilatation and edema by increasing capillary permeability, stimulate smooth muscle, provoke pain and are leukotactic. They are probably the hormonal mediator of the response to tissue injury because their concentration is increased at the sites of inflammation and when a synthetic kinin, bradykinin, is applied locally to certain tissues it mimics an inflammatory response.<sup>1</sup>

It appears that kinins are released from a plasma protein substrate by a plasma enzyme kallikrein and also by granulocytes. It appears further that blood clotting factor XII (Hageman factor) is involved in the process of kinin liberation and this explains how kinin release and the initiation of the clotting mechanism are closely linked processes. It is this process which has permitted Cline and Melmon<sup>1</sup> to examine the interaction between the kinin system and the anti-inflammatory steroids cortisol and prednisone to determine how they do this.

The final test system these authors used was to add washed granulocytes to the purified kininogen system (p.H.T.4). This caused liberation of biologically active kinins as the concentration of kinin-

ogen decreased. Cortisol added to this system partially inhibited the release of kinins. DOCA did not. Such observations suggested that cortisol in concentrations that are 4 to 8 times greater than physiological levels is capable of specifically interfering with the inflammatory response in vivo. The question remained whether the in vitro cortisol effect was an artifact.

This was examined by experiments on plasma obtained from patients receiving large doses of prednisone and from other patients not receiving prednisone. The results indicated that in the presence of prednisone plasma kinins were poorly released. Furthermore such patients had granulocytes which were much less active in liberating kinins. In short glucocorticoids administered to patients did in fact inhibit the formation of kinins from their plasma and this probably was the reason for their anti-inflammatory response.

One can think of two likely mechanisms of cortisol action in preventing kinin liberation thereby suppressing the inflammatory process. One is the inhibition of leucocyte activation of the kininogen system and interference with kallikrein the enzyme that converts kininogen to kinin. The other is interference with the interaction between enzyme and kininogen. The authors tested each of these possibilities and concluded that at least one site of cortisol action appears to be to prevent the enzyme kallikrein from acting on kininogen.

The most attractive hypothesis heretofore offered to explain the anti-inflammatory action of cortisol was "stabilization of lysosomal membrane with consequent inhibition of the release of irritating hydrolytic enzymes." If this hypothesis were correct then cortisol could never be anti-inflammatory in the doses used clinically.<sup>2</sup> Furthermore, anti-inflammatory steroids inhibit the early phenomena of inflammation such as capillary dilatation, edema formation, fibrin deposition, and migration of phagocytic granulocytes into the inflamed area. Such effects can hardly be explained by the effect of steroid on lysosomal membranes.

A more reasonable explanation is offered by Cline and Melmon. Cortisol and similar steroids probably exert their anti-inflammatory effect by preventing formation of vasoactive kinins which are responsible for many of the manifestations of acute inflammation. This effect of cortisol occurs at concentrations that can be achieved by drug administration.<sup>3,4</sup>

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## Calcium Ion In Clinical Medicine

Calcium has long been known to be one of the essential ingredients of life and a number of most fundamental biologic processes are absolutely dependent on its presence, such as blood clotting, fertilization, muscular contraction and normal nerve transmission. Calcium also confers upon individual cells in a multicellular tissue an adhesiveness which joins them together into a functional and structural whole and without which the cells would be a quivering mass of disconnected elements. It does for union of individual cells what the connective system does for tissues and organs.

We are all aware of the striking effects of changes in extracellular ion concentration upon almost all cells and organs in the body. The profound effects of calcium upon cellular function is dramatically illustrated by Lemann's<sup>1</sup> report on the severe and often fatal consequences of hypercalcemia as seen in patients with hyperparathyroidism. Conversely a reduction of calcium ion content of the blood results in an increased excitability of muscular and nervous tissue, gastrointestinal spasms, contraction of skeletal muscles lead to tetany. Tingling and a sensation of tension may begin in face and hands and spread to lower extremities and trunk.

Because the role of calcium in cellular processes is complex and still not well understood there has been increasing interest in studying the nature of these effects upon isolated tissues, cells and also such cellular systems.<sup>2</sup> Recent studies show that nearly all the intracellular calcium is bound to membranes either microsomal or mitochondrial and that a significant percentage of the intracellular calcium may actually exist as a phosphate salt within the mitochondria. The amount of calcium within the cell however is much less than it is in the extracellular fluid and this means that active mechanisms exist to maintain this concentration difference. In view of the close association of calcium and membranes, it is not difficult to realize why most of the effects of calcium upon cells have been related to its effects upon membranes.

It is now possible to discern at least two general functions of calcium in cellular activity. The first is related to its role in the cell membrane of controlling its permeability and electrical properties. The second is that of serving as a coupling factor

between excitation of cells. In muscle the coupling is between excitation and contraction. In glandular cells it is coupling between excitation and secretion.

Increases in extracellular calcium concentration increases what Rasmussen calls the "tightness" of cell membrane. This in turn leads to a decrease in the rate of flux of various ionic molecules across the membrane. For example hypercalcemia interferes with the transport of urea, sodium, and water across amphibian skin and amphibian urinary bladder. In the renal tubule calcium excess interferes with reabsorption of sodium, and uptake of glycerol. These effects may well be the primary bases of the polyuria, inhibitions of pitressin action and loss of concentrating ability observed as one of the invariable and serious consequences of hypercalcemia.

There is also decreased movement of sodium and potassium across plasma membranes and this probably explains the depression of membrane excitability, decreased muscle tone, and decreased responses of muscle and nerve membranes which are brought by calcium excess. Perhaps these alterations are the basis for the disturbances of nervous or mental functions which are such common findings of hypercalcemia in vivo.

If this explanation is correct than one would suppose that a reduced calcium in the blood would produce large open pores in the membrane, allowing easier interchanges between blood and cells of sodium potassium and perhaps also efflux of enzymes and other intracellular elements into the blood stream. Calcium then could be considered the guardian of intracellular elements from exuding out into the blood stream. The implications of this dire situation staggers the imagination.

The process of coupling appears to consist of a depolarization of the cell and microsomal membranes, and an alteration in their properties leading to the release of membrane bound calcium which in turn activates the contractile process.

The direct role of calcium as a coupler between stimulus and secretion in glandular tissue has been most clearly demonstrated in the case of the adrenal medulla where the release of acetylcholine at the splanchnic nerve-endings leads to calcium release and entry into the adrenal medullary cells with resulting secretion of catecholamines. Calcium has also been implicated in the secretory activity of other glands as well as hydrochloric acid secretion by the gastric mucosa.

Rasmussen reminds us that the role of calcium in hormone and drug actions is not confined to acetylcholine action, but also in the action of ACTH upon adrenal steroid genesis, the activa-

tion of AMP release by epinephrine, the action of vasopressin upon the renal tubule, the activation of phosphofructokinase by serotonin and the action of oxytocin upon the myocardium.

Many of the effects of calcium are antagonized by either potassium or vasopressin upon the heart. Calcium ions cause exactly the opposite effects of those of potassium ions resulting in markedly increased strength and duration of contractions. Greatly diminished calcium concentration in the extra cellular fluid can result in an extremely weakened heart<sup>3</sup> similar to that which results from potassium excess. Either a high potassium or a low calcium leads to an increased rate of breakdown of organic phosphates particularly those possessing high energy phosphate bonds. They play a regulatory role in pacemakers controlling glycolysis, respiration or both. Thus these changes may be the basis for weakening of the myocardium in states of hypocalcemia. A comprehension of the interrelated effects of changes in ionic composition is therefore necessary for any clear definition of the role of calcium in cellular activity.

The manner in which calcium exerts such effects is not yet clear. However, recent studies concerned with calcium ion accumulation in cells and subcellular systems make it clear that in most mammalian systems calcium is transported across membranes as a phosphate salt. This means that shifts in calcium across cellular and subcellular compartments and the consequent changes resulting from this movement requires an obligatory shift also of phosphates.

The complex interplay of the diverse effects related to calcium are becoming more clear and should be clearly defined by further study.

L.H.N.

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## Asphyxia, Seals And Man

There is a basic unity among living forms so that knowledge concerning any form enhances understanding of all living forms. We learn from the earthworm and snail how the original influenza epidemic spread. We learned from enterobacteriaceae how bacterial resistance to antibiotics may be transferred from one species to another. We learned from the cell-virus system of escherichia

coli a possible approach to cure of virus induced cancers. It is therefore not surprising that study of living animals and hibernating animals in their normal pattern of existence may throw light on our own capacity to cope with asphyxia and oxygen depletion.

The fresh water turtle can stay under water for twenty-seven hours and survive. The duck and the Harbor seal can stay under water for twenty minutes without any external oxygen supply, depending for their survival upon the oxygen in their lungs and blood.

It has been known for one hundred years that the duck when diving underwater experiences slowing of the heart rate from one hundred to fourteen beats per minute during a seven minute dive. This bradycardia is vagal in origin since it can be eliminated by cutting the vagus or administering atropine. Bradycardia apparently must have an advantage during asphyxia. We see this in the asphyxia of the new born as well as in the diving seal. With the onset of diving the heart rate drops from one hundred and fifty to ten. Robin<sup>1</sup> and Elsner<sup>2</sup> both describe this dramatic response which can be switched off and on by manipulating the animal.

Other primary adaptive responses which permits prolonged diving are generalized arterial constriction involving the vascular beds of all organs except the brain and heart. The degree of arterial constriction as shown by Robin, using angiographic techniques is so extreme that it is as if the involved organs were surgically removed from the animal. Blood flow in all peripheral areas ceases but flow to the brain continues. Similarly Elsner saw intense vasoconstriction in the exposed mesentery of the seal during immersion and almost total absence of renal flow. This seems to be the pattern in all diving animals. It seems clear that the widespread and selective vasoconstriction which occurs during diving provides for continued oxygenation of the brain and heart at the expense of organs of greater anaerobic capacity such as muscle, intestine, kidney.

Animals are fortunate that some of their parts can get along without oxygen for prolonged periods. Limbs can be deprived of oxygen by a tourniquet for as much as an hour without permanent damage. The muscles use up the oxygen stored in their myoglobin. Anaerobic energy from glycogen breakdown keeps the muscles alive. The resulting lactic acid accumulates in the muscle, can't get out into the blood stream because of a virtual shut off of the circulation to them. This protects the brain from the hypercapnia that would force involuntary breathing.



If the peripheral circulation ceases, venous return greatly declines and so does cardiac filling. Only blood from the brain and heart keeps flowing and this is why cardiac output greatly declines. Ordinarily we have here reproduced what happens in hypovolemic shock with the important difference that in shock cardiac acceleration is the rule, in diving profound bradycardia is produced to spare the heart from rapid exhaustion.

Similar findings are reported by Elsner in experienced divers who uniformly develop bradycardia not on breath holding, but on immersion. The heart rate may fall to as low as thirteen per minute, the limb blood flow fell almost to nothing. The difference between man and harbor seal is of course man's inefficiency to deal with asphyxia. In this respect man may be regarded as an inefficient seal. It appears that sensitivity of the respiratory center to  $\text{CO}_2$  is substantially less in the seal than in man. As a result asphyxia in this animal does not evoke the same urgency to breathe as would otherwise be true and so his diving can be prolonged.

This depressed respiratory center reminds us of a similar situation on clinical medicine particularly the patient with obstructive lung disease and hypercapnia. Such patients likewise have a depressed response to  $\text{pCO}_2$ . We may consider that this depressed response fulfills the functions of decreasing the volume of ventilation thus decreasing the work load and cost of breathing.<sup>3</sup> It also diminishes the sense of air hunger which would cause undue suffering in the victim. However the reduction of sensitivity of the respiratory center is not an unmixed blessing for it represents a type of disadvantage because a high  $\text{pCO}_2$  leads to lowered  $\text{O}_2$  tension.

The similarity between the diving phenomenon and the physiological events associated with hibernation is impressive. In the ground squirrel and the hedgehog onset of hibernation is associated with fall in heart rate, peripheral vasoconstriction, and much decreased cardiac output. During arousal normal circulation is more rapidly re-established in the heart than in the more peripheral parts of the body. These findings suggest a co-ordinated precisely controlled cerebral mechanism in hibernation similar to but having a much longer time course than those seen during diving.

We see then that the circulatory system plays a major, probably a dominating role in adjustment to the general phenomenon of asphyxia. Apnoeic diving is a special highly developed instance of this. The associated changes in cardiac function and peripheral circulation are among the most profound ever demonstrated by naturally occurring

stimuli. In addition to the precise neural control of the circulatory system, there are other abilities of animals that we must recognize as they cope with oxygen depletion. In the final analysis there must be adaptations occurring at the cellular level that permit adequate generation of energy despite low oxygen tensions.<sup>1</sup>

In both seals and man the relation between oxygen depletion and cellular function is poorly understood. We know the brain cannot survive after a brief period of oxygen deprivation. But peripheral tissues can. How do they do this? This area has been neglected and we may anticipate that this area is now the one in which major advances in understanding will occur during the next several years.

L.H.N.

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## Hyperuricemia An Important Threat In Hypertension

One of the intriguing questions we physicians encounter in dealing with hypertensive patients is why it is that some remain stationary in their hypertension while others go on to renal failure and accelerated hypertension. If we could recognize an element in a hypertensive patient that contributes to renal disease we would take the first step in preventing or at least showing the development of renal damage.

One clue to this problem comes from observations of long standing that antihypertensive therapy leads in many patients to the development of hyperuricemia. In Cannon's series<sup>1</sup> two-thirds of his hypertensive patients receiving thiazide drugs were hyperuricemic. What was however more striking was that thirty-eight of one hundred and nineteen patients with untreated hypertension who had elevations of serum uric acid. A further extension of this study revealed that in all hypertensive patients with hyperuricemia there was a reduced uric acid clearance by the kidneys. Obviously hyperuricemia is an important complication of hypertension in both treated and untreated patients.

In untreated hypertensives there was a direct relation between hyperuricemia and the occurrence of azotemia. As the BUN rose to forty-one so did uric acid rise also while in untreated primary hy-

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pertensives 22 per cent of fifty-four patients with normal BUN were hyperuricemic. With renal failure the incidence rose to 73 per cent. Even without renal failure but in hypertension with azotemia the incidence of hyperuricemia increased to 63 per cent.<sup>2</sup>

If one examines renal tissue post-mortem in patients who had become hyperuricemic during the course of hypertensive disease one finds changes like those seen in gouty kidneys even though the patients did not suffer from gout. The kidneys showed glomerular capillary thickening and sclerosis, tubular atrophy, pigment deposit, degeneration in the loop of Henle and extensive interstitial deposits of uric acid in the renal medullary tissue.<sup>3,4</sup>

The incidence of hyperuricemia in a healthy population has been estimated to be between 4.5 to 12 per cent. In Cannon's study 47 per cent in a total population of two hundred and seventeen patients with hypertension suffered with hyperuricemia. Such data clearly suggest that hyperuricemia in hypertension is not related to genetic factors operating in primary hypertension or to the etiology of underlying renal disease in renal hypertension. Cannon believes his data suggests that uric acid may be produced in some way by the hypertensive process itself.

However one should know whether other accompaniments of the hypertensive process could be related to the high incidence of elevated serum uric acid levels. Hypokalemia was not found in these patients and this makes it unlikely that hyperaldosteronism is implicated. There was an associated hypercholesterolemia which was even higher in this series than was the uric acid level. This however need not imply a specific etiologic relationship because the opposite was also true; the incidence of hypercholesterolemia increased among patients with elevation of serum uric acid.<sup>5</sup>

Hyperuricemia in hypertension could result from over productions of uric acid such as occurs in gout and familial hyperuricemia. It could result from impaired renal excretion of uric acid, perhaps secondary to the damaged kidney function associated with hypertension. The over production theory is unlikely since unsuspected gout is rarely found in this group. Cannon's data does not exclude the possibility of increased uric acid biosynthesis. But more likely is reduced renal excretion as the actual mechanism since hyperuricemia occurred in renal diseases which are not genetically linked. This hypothesis is also supported by the increased incidence of elevated serum uric acid in both types of hypertension with azotemia or antihypertensive treatment. The hypothesis that

renal uric acid excretion is reduced in hypertension and that it is this which leads to elevated uric acid levels, is supported further by the finding of a low uric acid clearance in fourteen of seventeen hypertensive subjects studied.

One other possible explanation of the elevated serum uric acid in hypertensives is the role of lactate. If one infuses lactate it is known to reduce the renal excretion of uric acid in both normal and gouty subjects.<sup>5</sup> In addition elevations of blood lactic acid has been associated with reduced uric acid excretion and hyperuricemia in normal subjects, during exercise, in glycogen storage disease and in toxemia of pregnancy.<sup>2</sup> In ninety-six of Cannon's patients the venous lactic acid level was significantly elevated to 27 mg. per cent as compared to 17 mg. per cent in forty-seven control patients.

Why do the hypertensive patients have elevated lactic acid levels? It occurs in both primary and renal hypertension. Is it a metabolic derangement or can it be due to anoxia caused by widespread peripheral vasoconstriction characteristic of the hypertensive process? Is the amount of lactic acid elevation sufficient to interfere with the reduced urate excretion. Clearly we have more to learn about this phenomenon.

The occurrence of hyperuricemia in a large fraction of the hypertensive population is probably produced by diminished renal excretions of uric acid.<sup>6</sup> The question might well be posed whether once hyperuricemia is established in hypertension it contributes to the deleterious effects of the hypertensive vascular disease in the kidney. The renal changes that were seen in tissue from three non-gouty patients with hypertension did resemble changes reported in renal tissue from gouty subjects. Such changes are not ordinarily seen in kidney sections from hypertensive patients in the absence of hyperuricemia.<sup>4</sup>

The findings therefore raise the possibility that high concentrations of uric acid in the renal blood and in the glomerular filtrate of hypertensive patients was precipitated in the renal medulla induced degeneration and inflammation and contributed thereby to the renal damage and functional impairment that accompanies hypertensive disease.<sup>7</sup>

This knowledge has come at a particularly fortunate moment when allopurinol, a xanthine oxidase inhibitor has been made available to the profession. Whether the hyperuricemia is primary or secondary this drug can reduce the level of uric acid in the blood and spare the kidneys of hypertensive patients with hyperuricemia from damage that results from urate deposition. Previously the



only method to deal with hyperuricemia in hypertension following treatment with thiazides was to use KCL and  $\text{NH}_4\text{CL}$ . We may reasonably expect that the glomerular sclerosis, renal tubular atrophy, degeneration especially in the Henle loops and uretral urate deposits will not occur on this regimen. If we can arrest the progress of hypertensive disease in the kidney we should prolong life and reduce premature invalidism.

L.H.N.

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## How Successful Is The "Pill": Family Planning In 1965

The birth rate in the United States has fallen by more than 20 per cent in the last eight years. This trend can only be interpreted if one obtains detailed information from responsible couples. It is appropriate to study this trend because our nation now faces problems which are related to population, such as poverty and race. The last inquiry on fertility was undertaken in 1960, the year when Enovid the first oral contraceptive was licensed for general use.

The first question is the extent of acceptance and use of oral contraception by the total population and also by its demographic and social subdivision. Accordingly a survey was conducted among married women born since 1910 and currently living with their husbands.<sup>1</sup> Interviews were carried out in 4,808 woman under age forty-five on their use of contraceptives. There were white women under forty-five. There were twice the actual representation of negroes in previous studies. A half sample of women forty-five to fifty-four has been added in order to provide the first substantial basis for quantifying the termination of reproduction by menopause in a natural sample.

The most important information was tabulated in regard to past, present and prospective use of contraception by age, fertility, number of live births, color, religion, education of married women under forty-five and living with their husbands. It does not contain sterile or pregnant women. It does not include consideration of oral contraception in relation to the use of other modes of fertility regulators. It is significant that only three per cent of all women had not learned about oral contraceptives or the birth control "pill."

The authors estimate that four million married women under forty-five and living with their husbands were using the "pill", 6.5 million have used it and another five million indicated they would use it in the future. This is probably an understatement because the figure excludes women over forty-five, never married women, women whose marriages have been interrupted and those who use the pill for regularizing the ovulatory cycle.

The use of the "pill" seems to be much greater among women under thirty of whom 40 per cent have already used it. This is a sharp increase over the 1960 survey for a variety of reasons. Young couples are likely to be especially attracted to a procedure which may enhance rather than inhibit sexual satisfaction. As age rises from under twenty to older periods, couples already have a family and are ready to terminate childbearing. Some women also use the "pill" for timing the birth of their first few children. Still others start using the "pill" after they have more than the desired number of children perhaps because other methods have proved unsuccessful. The greatest current use of the "pill" occurs among women who are still young and who have two children. The least current use not surprisingly is among women of advanced age in the lower parity groups.

Education seems to be an important variable, 22 per cent for college graduates, four per cent for individuals with less than a high school education. Such differences probably reflect the greater awareness and receptivity to innovations which is generally cultivated by education.

The data on age and amount of education are important because they provide indications of future behavior in the areas of reproduction and contraception as the proportion of newer women with more education increases. Already the majority of women with a college education have used the "pill" and it is estimated that three quarters will come to do so.

Negroes seem to be using the "pill" at a later stage (over twenty-five) than whites. This presumably is due to efforts to terminate rather than to time births. In the same education division there

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is little difference. It is, however, possible that Negroes did not learn of the availability of the "pill" as early as white women did. Some 10 per cent of Negroes did not learn about the pill as against three per cent of white women. In the south ignorance of the "pill" availability among Negro women rose to 14 per cent.

It appears a substantial number of Catholic women are turning to the "pill", 21 per cent under age forty-five, but only 15 per cent under age twenty. This suggests that Catholic women come to use the "pill" at a later stage in marriage than non-Catholics who are more likely to use oral contraceptives for timing births while Catholics for terminating theirs. The observation is as true for white as for non-white Catholics. Considering the persistent theological controversy about birth control, the report of Catholics who use the "pill" is substantial indeed. The differences which do exist in the use of the "pill" between Catholics and non-Catholics would probably disappear if the Catholic Church were to approve the use of oral contraceptives for purposes of responsible parenthood.

It would appear as though the oral contraceptive is likely to become the principle method of fertility regulators in this country. The high percentage among young non-Catholic college graduates is an extraordinary datum for a procedure not even available in 1960. We may of course expect changes in products used but the present "pill" has already transformed the pattern of fertility regulations in the United States.

The question of course is how much is the "pill" responsible for the downward trend in American births which began in 1957. To be sure this trend began before the first "pill" was first licensed as Enovid in 1960.<sup>2</sup> Nevertheless it has carried on and the young American wife now shares an extraordinary immediate enthusiasm for oral contraception as a means for achieving her reproduction goals.

We have for some time been deeply concerned about a vicious cycle of increasing birth rate and falling death rate and its trend to overpopulation in all countries of the world. Our hope is to stabilize the world's population and so to preserve at a decent level the quality of human life. Now for the first time the "pill" has brought within the realm of possibility widespread control of the world's birth-rate.<sup>3</sup>

At a time when many of the things we export to the world are held in dubious esteem, here is one export a means of world population control, already operating successfully in this country, of which we may justly be proud.

L.H.N.

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## Beta-adrenergic Stimulation In The Treatment Of Congestive Heart Failure: The Use Of Isoproterenol

Cardiac function in the normal and diseased heart is regulated by the amount of blood which returns to it per minute (venous return), by the heart rate, by the "Law of the Heart" (Starling's mechanism), and by the action of the beta-adrenergic receptors to the cardiac musculature. The venous return varies with many factors, being increased in exercise, expanded blood volumes and hypermetabolism, and decreased in shock and heart failure. The heart rate is generally under the control of the autonomic nervous system, being restrained by the vagus and accelerated by the sympathetics. When the rate becomes excessively slow as in Stokes-Adams syndrome, the heart overfills during the long diastole and the cardiac output falls. When the heart beats excessively fast, especially over 150 per min., then the diastolic period may become too short for adequate filling and here also the cardiac output falls and so does the blood pressure. The role of the beta-adrenergic receptors in paroxysmal tachycardia has already been clearly established.<sup>1</sup>

A third means by which cardiac function is regulated is by changing the stroke-volume output—(Starling's mechanism). The greater the heart is filled during diastole, the greater will be the force of cardiac contraction and the amount of blood pumped out. Thus the heart acts as an automatic pumping station to pump all the blood that comes to it from the veins regardless of how great or small this might be, so long as it is within the physiological limits of the heart. By doing this all the blood that comes to it is pumped out without allowing an excessive rise in end-diastolic pressure and venous pressure. When the end-diastolic pressure rises significantly, it is evidence that the Starling mechanism has been exceeded and the myocardial contractility is failing.

The most important factor that can change cardiac contractility is stimulation of the heart by the sympathetic nervous system. Such stimulation in-



creases the stroke volume output at each level of cardiac filling. Sympathetic stimulation therefore increases the effectiveness of the heart as a pump. However, it also increases the metabolism of the heart, and this is why its use in coronary artery disease must be approached with some caution to avoid angina pectoris.

As a result of these basic physiological principles it has recently been suggested that there may be a role for drugs that stimulate the beta-adrenergic receptors in the heart in the treatment of congestive heart failure and cardiogenic shock. Isoproterenol stimulates the beta-adrenergic receptors in the heart.<sup>2</sup> Thus by its direct effect on the heart it increases heart rate, the strength and velocity of shortening of myocardial fibers. This action results in augmented emptying of the heart with a decrease in the end-diastolic pressure and an increase in cardiac output. One might expect therefore that isoproterenol could partially reverse the hemodynamic abnormalities of congestive failure and other low cardiac output states.

It is not surprising therefore that Elliott and Gorlin<sup>3</sup> were stimulated to make a clinical trial of isoproterenol infusions on selected patients with congestive heart failure and low cardiac output states. They studied 91 patients during heart catheterizations in doses of 1 ug/min to 4 ug/min as a constant intravenous infusion. They measured heart rate, ejection period, cardiac output, ventricular pressures at rest and during the infusion.

There were no serious arrhythmias in the doses used. Almost all subjects showed some improvement in function with increased cardiac output, a lowered left ventricular end-diastolic pressure, increase in heart rate. The blood pressure, however, changed little, since the improved cardiac output was balanced by some peripheral vaso-dilatation. In two types of patients, those with aortic stenosis and coronary artery disease, no beneficial results were observed. In the former ejection is limited by an unyielding constricted orifice; in the latter, because the increased metabolism caused by isoproterenol was not matched by increased coronary flow. It would seem wise not to use isoproterenol on patients with failing hearts who suffer from aortic stenosis and coronary artery disease.

One of the mechanisms through which heart failure may be reversed by a catecholamine has been recently studied.<sup>4,5</sup> In congestive heart failure the myocardium and other tissues become depleted of their sympathetic neural transmitter nor-epinephrine and consequently such hearts are deprived of the cardiac reserve derived from sympathetic activity. There is now evidence that in the sym-

thetic nerve endings in the entire myocardium in heart failure there is an abnormality in storage and binding of nor-epinephrine. However, there is no impairment of end-plate receptor sites and the heart muscle often remains capable of responding if exogenous circulating catecholamines are made available to receptor sites.

Another mechanism that may contribute to development of heart failure is the use of reserpine or guanethidine or similar catecholamine depleting or sympathetic blocking agents which may further deplete nor-epinephrine stores.<sup>6</sup> With depletion of nor-epinephrine stores in the heart, reflex sympathetic activity can no longer evoke the extra performance required to compensate for intrinsic myocardial failure. However, if a catecholamine such as isoproterenol is available from the circulation the heart can still be driven to augmented function.

Isoproterenol (isuprel) was chosen rather than epinephrine because it has inotropic properties and virtually pure vaso-dilating properties which diminish the resistance to cardiac ejection. By contrast nor-epinephrine causes a sharp increase in arterial pressure because of its marked vaso-constrictor properties with production of hypertension and increased impedance of ejection as well as decreased coronary and renal flow.

It is likely that the greatest clinical usefulness of isoproterenol will be in the treatment of bradycardia, low cardiac output states, particularly following open-heart surgery, or in cardiogenic shock. The fact that this drug can be given sublingually will make it especially useful in chronic states requiring prolonged administration. It has been shown that massive doses cause myocardial necroses in rats.<sup>7</sup> We may rest assured that there is no evidence that doses employed clinically can injure the myocardium.<sup>8</sup>

L.H.N.

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## A Role For The Social Worker In The Private Practice Of Medicine

What does an internist do with a patient age fifty-six who has obesity and renal hypertension, but is overwhelmed by problems of sleeplessness, inability to make decisions and symptoms of increasing hypertension? How does he find out that part of her problem is caused by quarrelling with her daughter who is also actively engaged in the joint business venture? How does he go about discovering the basis of this conflict, to resolve them enough to lead to a lessening in the conflict which would greatly contribute to lessening the mother's anxiety?

What does a physician do now if he is confronted with a patient who is having marital difficulties that contribute to aggravation of a physical ailment? The marital difficulties seem to be related to a rigid personality of the patient as well as an unloving and recalcitrant wife. The patient's adjustment pattern raises the possibility of underlying psycho-pathology but a psychiatrist is refused. Would a psychiatrist be as well able to solve the marital trouble as an experienced social worker with whom the wife could share her concerns and who would respect her confidentiality? Would not removal of such difficulties add to happiness in a twisted family life and also reduce need for office visits to the doctor?

What does a physician do now with a patient who has a long history of rheumatic heart disease, has undergone a cardiac corrective operation, who is in despair over her marriage and doesn't know where to turn? Why is she in despair, what can be done about removing the causes? Obviously only a social worker could by expert interviewing uncover the patient's feeling of failure as a sexual partner, the husband's infidelity, discover the strengths and weaknesses, advise the physician about the need to educate the wife in sexual matters, and to remain on the alert for symptoms of stress.

What does a physician now do with a patient who has pains about the face and neck that come and go and seem to be related in some way to her inability to adjust to an apparently unsympathetic husband? The patient recognizes the need to do something with herself, to find work especially with children. She is, however, lost as to how to go about finding appropriate agencies who can help her to train and assume the useful role which she feels will allow her to "climb out of her box". How can the hus-

band be made to become sympathetic and helping instead of hostile and resentful of his wife's complaints? This is not the work of a psychiatrist but that of an experienced social worker who by skillful interviewing and knowledge of availabilities in the community could bring some kind of sympathy into a fractured relationship and assist a sufferer to some form of self-realization.

Social workers have been part of the medical team for many years and their contribution to good patient care in hospital settings and in agencies has been amply demonstrated. The problems mentioned above show how logical it is to extend the social worker services to the field of private practice. There is little doubt that the private patient treated in the doctor's office can derive both personal and medical benefit from the inclusion of social services in the overall patient management.

The social workers skill in the technic of interviewing is highly developed. The skills and time demanded for thorough exploration of a patient's social and emotional concerns are without doubt more at the command of the social worker than of the practicing physician. In addition social workers possess knowledge of available community resources and agencies and frequently have regular contact with the personnel who staff them. An area of especial competence useful in medical practice is the social workers ability to evaluate the cultural, ethnic and economic factors that affect illness.

A goal of the internist in private practice today is comprehensive medical care. Such care must often include attention to the emotional socioeconomic factors that may complicate effective treatment of the patient's physical problems. Since the physician bears primary responsibility for the patient's care, what is more logical than to develop a working relationship with social workers whose skills are indispensable to the doctor in certain situations and can be used effectively by the physician in alleviating physical and emotional and mental suffering.

Wegner, Ruiz and Caccamo<sup>1</sup> report on their experiences in just such an experiment in comprehensive care, having established a working relationship with a social worker. When faced with a patient involved in an explosive marital situation they brought a social worker into the office for consultation when the patient resisted referral to a community agency. The social worker promptly recognized the basis of the problem, successfully proceeded to solve it. The success of this initial experience resulted in a firm working relationship between the medical office and the social worker.

We all recognize that emotional and adjustment problems frequently complicate medical therapy. Many patients can compensate adequately for these concerns without outside help. It is those unable



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The following is a brief precautionary statement. Before prescribing, the physician should be familiar with the complete prescribing information in SK&F literature or *PDR*.

*Precautions:* Use with caution in patients hypersensitive to sympathomimetics or barbiturates and in coronary or cardiovascular disease or severe hypertension. Do not use in patients taking MAO inhibitors. Excessive use of the amphetamines by unstable individuals may result in a psychological dependence; in these instances, withdraw the medication. Use cautiously in pregnant patients, especially in the first trimester. *Side effects:* Insomnia, excitability and increased motor activity are infrequent and ordinarily mild.



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to do so for whom we must search for social workers who can reach to the basis of their problems and assist in their solution. Most patients will not wish to go to a community agency for fear of violation of their privacy and damage to social standing. With the active support of a physician a private social worker can establish a rapport with a referred patient since it is an extension of an already existing rapport with the physician. The patient realizes that the social worker is engaged in the handling of his problem which is not strictly medical.

Wegner's group resorted to the help of the social worker when a patient was unable or unwilling to follow medical recommendations resulting in unsatisfactory treatment progress. In some cases medical progress was good but stressful situations in the parents lives suggested the likelihood of future psychic or physical problems. Another group referred to the social worker were patients who presented little evidence of physical distress, but emotional and socioeconomic problems required the skill of the social worker, such as marital problems, adjustment to illness (economically, socially, psychologically), adolescent adjustment problems, family conflicts and those requiring psychiatric help, vocational counselling and placement.

From time to time the social worker and physician have met to discuss the patient's adjustment and medical progress. In some instances the social worker has alerted the physician to an urgent problem which might not have come to their attention until much later and which required an adjustment in medical therapy. In short the special competence of the social worker became an extension of the doctor's services.

The function of the social worker in the private practice of medicine is largely in the sphere of interpersonal relations such as adjustment to disability, personal maladjustment precipitated by a medical crisis situation. Most people in maladjusted situations will refuse referral to a psychiatrist but will readily accept the social worker as a supposed ally in coping with a recalcitrant spouse. Such problems are best solved by the social worker whose skill is to evaluate strengths and weaknesses in a family relationship after they have been uncovered.

The trend in medicine is to treat not only a sickness but the whole person. The skill of an associated social worker will add to medical practice an important dimension in the treatment of the whole person.

L.H.N.

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## An Editorial On Automobile Accidents

An editorial in the current *Journal of the American Medical Association* has this to say about automobile accidents:

"Directing attention to the 'nut behind the wheel' is worthwhile as long as we do not permit two fallacies to direct research policy. The first fallacy is that identifying all 'nuts' (however one defines the term) is possible.

"The second fallacy is that, even if possible, this identification could be used so as to prevent all or most traffic accidents.

"Collisions frequently are caused by momentary inattention, by sudden unpredictable changes in climate or road conditions, by faulty tires producing blowouts, and by poor automobile design or construction. These factors can involve the most careful and skillful driver in an accident.

"In a way, our attitude toward automobile safety in the past seems punitive. By ignoring research into more crashworthy vehicles, we seem to have been implying: if you are stupid enough, or criminal enough to be involved in an accident, you deserve the consequences."

More research is needed on the "second collision" in an auto crash, the editorial said. This second collision occurs when occupants strike the vehicle's interior after the car collides with another object.

"Despite general lack of interest in second-collision research a few individuals have worked on this problem," the editorial said. "They have shown that many dangerous features in our cars can be corrected at once, without further research.

"The interior of our cars must be stripped of sharp handles and protruding knobs. Adequate padding must be provided throughout the automobile. The chest-crushing potentiality of the steering column must be eliminated."

The number of persons who don't use their seat belts indicates how difficult it is to motivate drivers to protect themselves, the editorial said.

"Yet the belts seem unquestionably helpful in preventing significant numbers of fatalities, and there is further evidence that a combination seat-belt-shoulder-harness offers even more protection."

One of the many things physicians can do to help reduce highway deaths is to advise their patients, the editorial said. "They deserve to know what risks they take when they drive, and they deserve to know how necessary—or unnecessary—these risks are."



# MOLECULAR REMODELING—

*laboratory exercise or clinical necessity?*

More than twenty-five years have passed since the discovery of the diuretic activity of sulfanilamide started pharmacologists on a succession of molecular remodeling to find the ideal diuretic.

## Diuresis—a sought-after clinical effect from an unwanted side effect

It started in 1937 when a clinician reported that the administration of a sulfonamide was sometimes accompanied by an unexplainable side effect—metabolic acidosis.<sup>1</sup> Three years later the side effect was explained. The sulfonamide radical of sulfanilamide inhibited carbonic anhydrase,<sup>2</sup> the enzyme responsible for converting carbon dioxide and water to hydrogen ions and bicarbonate ions.

Later, other investigators showed by dog experiments that metabolic acidosis probably resulted when the inhibition of carbonic anhydrase upset the exchange of hydrogen and sodium ions, causing increased excretion of sodium as the bicarbonate.<sup>3</sup>

It was twelve long years after the first report of the unexplainable side effect (metabolic acidosis) that it was finally shown that large doses of sulfanilamide administered to edematous patients were indeed capable of promoting diuresis.<sup>4</sup> However, the possibility of toxic effects from its prolonged use and its relatively weak diuretic action made it impractical for clinical use as a diuretic.<sup>5</sup>

Because the inhibition of carbonic anhydrase seemed to be the key to effective diuresis, investigators began to look for more potent enzyme inhibitors—in the hopes that they would be more effective diuretics.

The most important of these early compounds, acetazolamide, enjoyed several years of fairly wide clinical use.

Its carbonic anhydrase inhibitory activity was several hundred times greater than that of sulfanilamide.<sup>6</sup> The increase in inhibitory activity, however, increased not only the excretion of sodium and bicarbonate ions, but also the excretion of potassium.<sup>7</sup> And, like its predecessor, acetazolamide precipitated mild acidosis. Its prolonged use could result in hypokalemic acidosis.<sup>7</sup>

## The 'thiazides'—an answer to the metabolic acidosis caused by carbonic anhydrase inhibition

Despite the fact that the sulfonamide

group appeared to be responsible for carbonic anhydrase inhibition which in turn appeared to be responsible for diuresis, investigators began to synthesize compounds with structural alterations to the sulfonamide group.

The first major breakthrough came with the synthesis of chlorothiazide. Altering the sulfonamide group did indeed alter the ability of chlorothiazide to inhibit carbonic anhydrase—it was only 1/10th as potent as acetazolamide in inhibiting the enzyme.<sup>8</sup> Despite the drop in inhibitory potency, however, chlorothiazide proved to be an effective diuretic—an observation that led to the conclusion that its diuretic action was due to some mechanism other than its action on carbonic anhydrase.<sup>9,10</sup>

For effective diuresis, chlorothiazide was administered in daily dosages ranging from 250 to 2000 mg.<sup>11</sup> It increased the excretion of sodium and chloride; and, to a lesser extent, potassium and bicarbonate.<sup>11</sup> The excretion of potassium appeared to be maximal at higher dose levels at which, theoretically, the carbonic anhydrase inhibitory effect is more active.<sup>11</sup> Its prolonged use, therefore, could sometimes result in metabolic hypokalemic, hypochloremic alkalosis.<sup>7</sup>

## Naturetin—effective diuresis with more favorable electrolyte balance

Other thiazides followed—with improvements being aimed at two particular areas: 1. attempts to increase diuretic action in relation to the milligram potency of the drug, and 2. attempts at a more favorable sodium/potassium ratio in the urine, i.e., to decrease the excretion of potassium while maintaining the excretion of sodium.<sup>12</sup>

One of these, Naturetin, Squibb Bendroflumethiazide, has made advances on both these points. "By adding a 3-benzyl radical to hydroflumethiazide a rather dramatic reduction in dose range is accomplished. With this drug, effective sodium excretion is obtained with

doses between 2.5 and 10 mg., which is a 200 to 1 ratio as compared to chlorothiazide..."<sup>13</sup>

Moreover, due probably to its virtual lack of carbonic anhydrase inhibition, Naturetin (bendroflumethiazide) has been shown to cause less potassium and bicarbonate loss and less alteration in urinary pH than either chlorothiazide or hydrochlorothiazide.

Naturetin is outstandingly effective not only in establishing, but also in maintaining, excretion of retained fluid in edematous patients. And its duration of action is sufficiently prolonged to allow a single daily administration in most patients. Naturetin is also an effective antihypertensive agent.

**Contraindications:** Severe renal impairment; previous hypersensitivity.

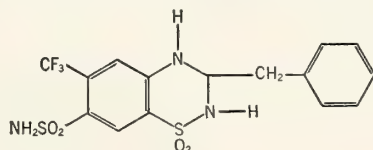
**Warning:** Ulcerative small bowel lesions have occurred with potassium-containing thiazide preparations or with enteric-coated potassium salts supplementally. Stop medication if abdominal pain, distension, nausea, vomiting, or G.I. bleeding occur.

**Precautions:** The dosage of ganglionic blocking agents, veratrum, or hydralazine when used concomitantly must be reduced by at least 50% to avoid orthostatic hypotension. Electrolyte disturbances are possible in cirrhotic or digitalized patients.

**Side Effects:** Bendroflumethiazide may cause increases in serum uric acid, unmask diabetes, increase glycemias and glycosuria in diabetic patients and may cause hypochloremic alkalosis, hypokalemia; cramps, pruritus, paresthesias, and rashes may occur.

**Supplied:** Naturetin (Squibb Bendroflumethiazide) 5 mg. and 2.5 mg. tablets. Also available Naturetin  $\bar{c}$  K [Squibb Bendroflumethiazide (5 or 2.5 mg.) with Potassium Chloride (500 mg.)]. For full information, see Product Brief.

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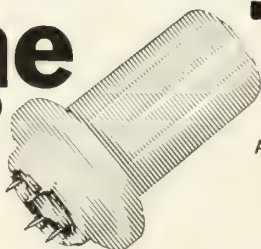
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# More Light On The Heritage Of Connecticut Medicine

Ira V. Hiscock, M.P.H., Sc.D.

■ That Health is a Community Affair, and Public Health is a Community Action Process, by people who are concerned, is emphasized in all of the forward looking 1966 reports of the National Commission on Community Health Services.<sup>1</sup> That physicians have rendered significant service in Connecticut's community action process for better physical, mental and social well being is recognized by all who are familiar with the Heritage of Connecticut Medicine.<sup>2</sup> Continuing evidence of this constructive service becomes impressive while observing new developments in rapidly changing conditions, and also while exploring further backgrounds and landmarks in the History of Connecticut.<sup>3</sup>

So much has happened for the benefit of people in 200 years, since 1763, when a group of Connecticut doctors petitioned the Legislature for a charter that would distinguish the "honest and ingenious" physician from the "quack"! So much is pressing for consideration now, due to new, exciting, opportunities which require partnership planning and cooperative action by statesmen, professional and nonprofessional, who care for people's health and happiness! While steps are being taken to meet the challenges of Medicine and to implement the provisions of federal and state legislation of recent months, we can derive satisfaction in reviewing illustrative lessons of the past.

In "The Generosity of Americans" is traced the private generosity for the public good as a distinctive and dynamic force in the creation of western civilization. Here is discussed why Americans give \$11 billion a year, channelled through over 975,000 private service and cultural agencies in the U.S., with 40,000,000 persons participating, to bolster current local, state and federal welfare, educational and health programs. People and agencies in Connecticut share liberally in this yearly activity. The beginnings of this social force originated in Europe and the Middle East, fostered "by the prophets in the Old Testament, by Christ, by the Catholic Church (called the "great conduit of generosity"), through Rome, and then imported into the new colonies in America by early settlers from England and the Netherlands."<sup>4</sup>

While many professional persons have not always been notorious for their financial contributions to community agency activities across the country, they have usually displayed a high degree of

generosity in rendering services; and there are striking exceptions, furthermore, in terms of money, dating back 150 years, as illustrated in Connecticut. In the light of recent reports of comprehensive plans for mental health<sup>5</sup> and for mental retardation<sup>6</sup> services in Connecticut, for example, of more than passing interest in showing human interest and in building foundations, is the report of a committee of the Connecticut Medical Society respecting an Asylum for the Insane, 1821,<sup>7</sup> and action thereafter.

An encouraging note of optimism is found in the *Promise of America*, an historical inquiry,<sup>8</sup> which gives a broad view full of pride and gladness at "those best hopes Americans have nourished," and of impatience at the times when we fall short of our national purpose.

An example from the State Medical Convention held in Hartford in May of 1821, gives some of the Connecticut and even New England atmosphere. Eli Todd had urged that insanity should come under the supervision of medicine, stating that it was only a manifestation of disease "as is a fever or a fracture." He urged instruction of delegates to the Convention the propriety of taking steps to establish an institution.

"Once before, in 1812, the Reverend Nathaniel Dwight, M.D., both preacher and practitioner of medicine, had presented a similar matter to the convention to no avail. This time, however, Todd's vision for an institution brought not only enthusiastic endorsement but an appropriation of two hundred dollars, then a sizeable amount, from the Society's treasury for a survey of the needs. The following October the Committee reported that approximately one thousand deranged individuals in the State of Connecticut were being cared for, often under conditions unbelievably barbarous. Then, as now, the Connecticut Medical Society felt and assumed a definite responsibility for individual and public health, and they emptied their treasury for the cause. A relief society was formed with sub-committees in every county in the State, the doctors joining with the outstanding clerics, business

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men, lawyers and society leaders in every county. . . . Donations ranging from twelve and a half cents to three hundred dollars were gathered in throughout Connecticut, Maine, Rhode Island, Vermont and Massachusetts. Nor was money the only contribution, for among the non-monetary gifts recorded there appears 'one gross of New London Bilious Pills, market price \$30.00.' By May, 1822, twelve thousand dollars had been paid in on pledges toward the proposed institution and "The Retreat" had been chosen as its name.

The influence of Todd and the Connecticut Retreat expanded, and when Dorothea Lynde Dix, "the prim New England school teacher, embarked upon her ambitious career she took unto herself three psychiatric "god-fathers" as her sponsors. Of these one was John S. Butler, Todd's successor at the Connecticut Retreat, another the same Sam Woodward whom he had placed at Worcester, and the third, Horace Mann."<sup>2</sup>

When young Horace Mann stood on the floor of the Massachusetts legislature and enunciated the principle that "the insane are the wards of the state,"<sup>9</sup> his thought was apparently quite removed from the present-day conception that state care includes provision in state-owned hospitals, administered and maintained by the state, for all mentally ill persons in need of public care and treatment.\*

In the remarkable document of the Sanitary Commission of Massachusetts of 1850, Lemuel Shattuck, and others included among their far seeing recommendations that the "authority now vested in justices of the peace, relating to insane and idiotic persons, not arrested or indicted for crime, be transferred to the local Boards of Health." By the existing laws of the State, no insane or idiotic person, other than paupers, could be committed to any hospital or place of confinement, except on complaint, in writing, before two justices of the peace or some police court. "It may be supposed," wrote Shattuck, "that such Boards will be better acquainted generally with the medical jurisprudence of insanity, than justices of the peace; and their decisions will be, more than those of criminal courts, in accordance with the spirit of humanity which has been extended to that class of persons."<sup>10</sup>

The modern public health movement in America dates from the period of significant reports from England by Chadwick and Simon and from Massachusetts by Shattuck, a little over 100 years ago. The opening decade of the present century was rich in the rise of reform movements—political,

economic and social. Development within the so-called field of public health exerted influence on the growth of the preventive ideal. Fielding H. Garrison, in his *History of Medicine*, refers to this period as the "beginnings of organized, preventive medicine." In this decade, Connecticut physicians were among those leaders who helped to produce such organizations as the National Tuberculosis Association 1904 (David R. Lyman); the American Social Hygiene Association 1910 (John Lane); the American Child Health Association 1909 (Joseph I. Linde); and The National Committee for Mental Hygiene, formally organized in 1909, though its inception dated one year earlier.

While the mental hygiene (health) movement developed out of the same broad forces that brought into existence similar movements in other fields about the same time, it was unique in origin, following the remarkable classic in auto-biography, *A Mind That Found Itself*, published in 1908, five years after its author's emergence from his round of mental hospitals.<sup>11</sup> Dr. Gustavus Eliot and Dr. Diefendorf were, among the small group who met with Clifford Beers and Wilbur L. Cross, and Anson Phelps Stokes in the latter's home at 149 Elm Street and voted to organize the Connecticut Mental Hygiene Society—the forerunner of the National Association.

Moving on through the years, on a solid foundation, with a promising goal, to 1965, Connecticut Medicine rendered essential advice in the development of the State Department of Health Plan for Chronic Illness and Aging Activities. Several members of the State Medical Society served constructively on specialized panels of discussion and on the advisory committee responsible for preparing a report. The Public Health Committee of the State Society continued to review and pass judgment and give suggestions on numerous new and old opportunities, as has been its characteristic of many decades. The pediatricians of the Academy and of the Society continued their wise guidance of affairs especially pertaining to maternal and child health, to mental retardation, and to health of school age children and teachers. Chairman of the Committee on Public Health of the Governors Clean Water Task Force was a local director of health and a busy practicing physician, in a small, wealthy state, where only about half of the people have the benefit of modern, full-time, health administration. The medical advisory committee of the State Welfare Department, where 40 per cent of expenditures in a year are for medical and drug purposes, includes several pediatricians.

In the preparation of the two basic plans for comprehensive mental health services for the communities of Connecticut and for Mental Retarda

\* The evolution of state care followed a long winding trail before reaching its significant expression with the passage of the New York State Care Act of 1890.



tion Planning, (which features Robert Frost's Miles to Go before I sleep: "The woods are lovely, dark, and deep, but I have promises to keep"), physicians in many specialties and in general practice participated actively. We have guide lines for action, in a widely informed public, who seek wise future action, for the benefit of all concerned. These and other important studies and deliberations give us a strong base from which to operate as we enter a new complex era of joint planning and cooperative action for the future.

As we review these and other stories illustrating how responsibility was assumed in meeting situations of earlier years, we may recall Justice Holmes' observation that "a page of history is worth a volume of logic." Can the complexities of partnership planning for wise utilization of provisions of Medicare, Titles 18 and 19 and others to come,<sup>12</sup> be more difficult than those which were met with courage and capacity in earlier years? Is there any ceiling in future promises for old and young? In Webster's Twentieth Century dictionary, Heritage means something handed down, the right, burdens, or status resulting from being born in a certain time or place; birthright. The image and status of physicians' leadership in Connecticut, Webster's cherished home, show confidence and skill in achievement. Osler used to urge doctors to take part in their county medical society affairs, to find first principles, to reason, to share gains, and, perhaps, to reinforce the urge to be, as the Passavant Hospital motto says, "More than yesterday, less than tomorrow." Both medicine and the people and families of the community can continue to benefit

in so many ways from cooperative endeavors while moving forward in the rapidly changing world.

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"Every man is not a proper champion for truth, nor fit to take up the gauntlet in the cause of verity."—Sir Thomas Brown

# The Allergic Patient

John R. Algird, M.D.

## Introduction

■ The avoidance of allergic reactions is one of the most important services a physician can render his patient. A careful history coupled with a high index of suspicion can eliminate allergic reactions in sensitive patients. This avoidance of predictable reactions is mandatory in view of an ever increasing incidence of suits for malpractice. This category of patients should include not only those who are truly allergic, but also those who exhibit a hypersensitive or abnormal response to any given medication.

## Method

In order to determine the incidence of allergy or hypersensitivity to drugs or other agents, the consecutively numbered records of 1,000 patients admitted to the private wing of The Free Hospital For Women were examined. Those patients were considered allergic or hypersensitive whose histories were clear cut or suspicious enough to be considered so by the staff anesthesiologist who interviewed the patient. For example, the patient who exhibited a vesicular eruption several hours after application of adhesive tape was included in this category as was the patient who exhibited edema of the face and extremities as well as a generalized urticarial reaction after the parenteral administration of penicillin.

## Results

From Table I, it is evident that allergic histories are very common, if one specifically seeks them out. The over all incidence of 149 per 1000 cases indeed emphasizes the necessity of a good medical history. Furthermore, the predominance of penicillin allergy, accounting for 48 per cent of the total allergies should lead to careful thought before routinely ordering this antibiotic.

## Discussion

Stetler and Moritz<sup>7</sup> state that because a patient has an allergic reaction to medication does not ordinarily infer negligence upon the part of the physician. This is particularly true when the allergy manifests itself for the first time. However, should the physician either fail to question his patient

concerning any known drug allergy, or having elicited a known drug allergy, inadvertently administer that drug to his patient, his vulnerability in a court of law becomes most marked. Here the doctrine of "common knowledge" might be applied. This doctrine is related to but differs somewhat from the doctrine of "res ipsa loquitur". It permits a jury to find a physician negligent, upon proof of an injury to a patient, caused by an act or omission on the part of the physician, without medical testimony to establish the applicable standard of medical care, where the jury from its fund of common knowledge can determine the proper standard of care.

In view of the fact that skin testing to determine sensitivity to many drugs is of little value,<sup>6</sup> the physician's optimum protection remains in obtaining an accurate history of known allergies. The possibility of cross reactivity of certain groups of drugs should be remembered and medications having a different chemical configuration should be substituted.

The variety of agents capable of producing an allergic reaction are legion. Ethan Allen Brown<sup>2</sup> very aptly sums up this bewildering array, stating, that "those agents which readily come to mind may be derived from other humans, anthropoids, other mammalian, avian, ichthyic, reptilian, insect, vegetable, bacterial, fungal, rickettsial and viral sources as well as the permutations and combinations of all of the inorganic elements of the periodic table in addition to synthetic drugs, sometimes imitating and sometimes non-existent in nature. These may be ingested, inhaled, injected, inserted, instilled and applied as liquids, pellets, grafts, aerosols, suppositories, nebulae, unguents and powders, for deposition on or absorption through every portion of the skin, mucous membranes or tissues of every available system of the body."

No attempt is made to discuss all the drugs listed in Table I. The following comments on a few of the agents listed in Table I seem to be pertinent.

Pencillin is the drug most frequently producing allergic effects. The response may be immediate consisting of urticaria, rhinitis, asthma or ana-

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TABLE I  
HISTORY OF ALLERGY OR HYPERSENSITIVITY IN  
1,000 CONSECUTIVELY NUMBERED HOSPITAL ADMISSIONS

|                      |     |
|----------------------|-----|
| Penicillin           | 72  |
| Sulfonamides         | 16  |
| Meperidine           | 12  |
| Codeine              | 12  |
| Horse Serum          | 7   |
| Barbiturates         | 5   |
| Morphine             | 5   |
| Procaine             | 4   |
| Adhesive Tape        | 3   |
| Acetylsalicylic Acid | 3   |
| Others (One each)    | 10  |
| Total                | 149 |

phylactic shock. Severe reactions may end fatally.<sup>3</sup> Symptoms may simulate those of serum sickness; urticaria, angioedema, arthralgia, and frequently fever. The latter usually appears 7 to 10 days after administration of the drug and persists for two to four weeks. However its duration is extremely variable and may last from a few hours to a year. Another reaction is that of contact dermatitis. This is usually the result of topical applications or exposure to aerosols.

A history of penicillin allergy should suggest the possibility of allergy to procaine, because of the almost universal use of procaine penicillin. Seigel and Adelman<sup>6</sup> reported three patients with penicillin hypersensitivity who exhibited localized edema at the site of injection. Subsequent testing showed that two of these three patients were also sensitive to procaine. Once sensitivity to para-amino-benzoates has been established, it should be remembered that many sunburn lotions and creams contain members of this class of drugs.<sup>4</sup>

Sulfonamides are the second most frequent cause of allergic reactions. Berman<sup>1</sup> has shown that practically all the major dermatoses known to man have at one time or another appeared in patients allergic to sulfonamides. These include eczematous, ery-

thema-multiforme like, erythema-nodosa like, fixed eruptions, lichenoid, pemphigoid, and ulcerating eruptions, purpuric, scaly and exfoliative eruptions, urticaria and angioneurotic edema.

The policy of the hospital staff is to avoid using any of the sulfonamides if a previous allergic response has been established. Other antibiotics are utilized to achieve the desired therapeutic effect.

Of interest to the physician is the small group of patients who exhibit a hypersensitivity to adhesive tape.<sup>5</sup> The use of the new hypoallergenic adhesives has almost entirely eliminated this annoying problem.

### Summary

It is contingent upon the physician to obtain an accurate history from patients with a suspected allergy, bearing in mind the possibility of cross reactivity of certain groups of drugs. Skin tests are not sufficiently precise to be of value prophylactically.

The drug responsible for most allergic reactions in our series is penicillin (7.2 per cent). Sulfonamides accounted for 1.6 per cent of the total. These two drugs are capable of producing most of the major dermatoses known to man.

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# Enterovirus Infections In Connecticut

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■ Within recent years, the extensive use of tissue culture techniques for virus isolation and serologic procedures has made possible the identification of over 60 distinct enterovirus serotypes responsible for human infections. Clinical manifestations associated with various members of the enterovirus group range from relatively mild, undifferentiated, febrile illness to severe paralysis and death. The purpose of this report is to review recent knowledge on the classification of enteroviruses, the laboratory diagnosis of enterovirus infections and the clinical syndromes caused by various enterovirus serotypes. In addition, studies on enterovirus infections conducted at the Connecticut State Department of Health Virus Laboratory during a six year period from 1960 through 1965 will be described. Information will be presented on the yearly variation, seasonal distribution, laboratory diagnosis and clinical diagnosis of enterovirus infections prevalent in Connecticut during the six-year period.

## Classification of Enteroviruses

The term "picornavirus" (small-ribonucleic acid-virus) was recently proposed by an International Enterovirus Study Group as a new name for a group of viruses with common biochemical and biophysical properties.<sup>1,2</sup> The picornaviruses were defined as viruses which (1) are small in size (15 to 30 millimicrons in diameter), (2) are insensitive to inactivation by ethyl ether, and (3) contain ribonucleic acid. The group contains a large number of distinct serotypes (probably 100 or more infect man alone) and includes etiological agents of a number of important diseases of man and animals.

Within the picornavirus group the following biological subgroups were recognized:

### 1. *Picornaviruses of human origin*

#### a. Enteroviruses

- (1) polioviruses, type 1-3
- (2) coxsackieviruses A, types 1-24\*
- (3) coxsackieviruses B, types 1-6
- (4) echoviruses, types 1-32\*\*

\* Coxsackievirus A, type 23 was never formally accepted as a new type since it was found to be identical with the previously described echovirus 9.

\*\* Echovirus, type 10 (reovirus) was removed from the group when it was shown to be a larger RNA virus; echovirus, type 28 is now considered to be a rhinovirus.

*Laboratory studies conducted from 1963 through 1965 were supported in part by a National Vaccination Assistance Project Grant.*

b. Rhinoviruses (common cold viruses)—over 30 types

c. Unclassified

### 2. *Picornaviruses of lower animals*

Unclassified

Members of the enterovirus and rhinovirus subgroups differ from each other in acid stability, cytopathogenicity for tissue cultures, and temperature requirements for optimal growth. Viruses isolated from simian, bovine, porcine, murine and other species of lower animals will be classified into subgroups similar to the human picornavirus subgroups when more information about these animal viruses is obtained.

## Diagnosis of Enterovirus Infections

*Clinical specimens:* The proper collection, storage and shipment of clinical specimens are essential prerequisites for successful enterovirus cultural and serologic studies. Specimens required for this group of viruses are (1) acute stage feces and throat swab specimens for cultural examination and (2) paired serum specimens for serologic examination. The acute serum should be collected from 1-5 days after onset of disease and the convalescent serum from 10-21 days after the acute specimen. If an acute serum is not available, paired convalescent serums collected about two weeks apart may be submitted for testing. Postmortem specimens should be collected under aseptic conditions and stored in the frozen state until examined (except postmortem whole blood which should not be frozen for serologic studies). The source of the material depends on the type of clinical disease and in general those organs suspected of harboring viruses or showing gross pathology are submitted for examination. All specimens for cultural studies should be frozen or refrigerated after collection and shipped to the laboratory frozen in dry ice, or if freezing facilities are not available, the specimens should be transported to the laboratory within a few hours after collection chilled in wet ice. Acute and convalescent blood or serum specimens may be shipped through the mail without refrigeration (appropriate shipping containers and detailed directions for collecting and shipping specimens may be obtained upon request from the Laboratory Division of the Connecticut State Department of Health).

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*Virus isolation methods:* The animal and tissue culture test systems employed for the isolation of enteroviruses are shown in Table I. Rhesus monkey kidney cell cultures are used routinely in most virus diagnostic laboratories for the isolation of enteroviruses because they are (1) susceptible to a wide range of enteroviruses (2) available commercially at a reasonable cost (3) relatively resistant to toxic factors in clinical specimens and (4) easily maintained for a two to four week test period.

The polioviruses, group B coxsackieviruses and echoviruses grow well in monkey kidney tissue cultures and produce a characteristic cytopathic effect which aids in their identification. Infected cells round up, become refractile, eventually degenerate and fall off the glass surface on which they have been grown.

These viruses also produce characteristic plaques in monkey kidney cultures which have been stained with neutral red and overlayed with agar. Polioviruses produce circular, large plaques with clear centers and sharp boundaries. Plaques of coxsackie B viruses are round, resembling those of poliovirus, except that they have rather diffuse boundaries and their appearance is delayed. Echovirus plaques are usually small, irregular and delayed. A variety of primary human cell cultures (kidney, lung, amnion) and continuous human cell lines (HeLa, HEp-2, KB) are used in conjunction with monkey kidney cultures, but none are as suitable as the latter cultures for primary isolation work.

The majority of the group A coxsackieviruses do not proliferate in monkey kidney tissue cultures (coxsackievirus A9 is an exception) and produce only a limited cytopathic effect in human tissue cultures upon primary isolation. The host of choice for this group is the suckling mouse. Group A viruses produce in newborn mice a generalized myositis accompanied by a flaccid paralysis. Enteroviruses isolated in tissue cultures or suckling mice may be typed serologically for final identification in neutralization, complement fixation or hemagglutination inhibition tests.

*Serologic methods:* The neutralization test is the procedure of choice for demonstrating significant antibody increases or decreases (fourfold or greater) in paired serum specimens (Table I). The complement fixation and hemagglutination inhibition tests are not as widely used for the serodiagnosis of enterovirus infections because these tests are less specific than the neutralization test and potent complement-fixing and hemagglutinating antigens are not available for the majority of the enteroviruses. The neutralization test is based on the principle that when a specific immune serum is added to its corresponding virus, the virus is rendered non-infective or is "neutralized". Since demonstration

of infectivity requires the use of living tissues, the host systems employed are usually those in which the virus proliferates best. In practice, serial dilutions of the patient's acute and convalescent serums are mixed with a standardized dose of infectious virus. The virus-serum mixtures are usually incubated at room temperature for one hour and then inoculated into tissue cultures or suckling mice. The neutralizing end point or titer of the serum is expressed as the highest dilution of serum which protects the host against infection. Since the enterovirus family now consists of more than 60 members, neutralization tests are generally carried out only with selected members of the group which are currently active in a community.

*Clinical syndromes:* The portal of entry of the enteroviruses is the alimentary tract. After initial multiplication in the lymph nodes, viremia may occur and may lead to further virus proliferation in the cells of the reticuloendothelial system, and finally to a more serious infection of other organs (meninges, myocardium, skin, CNS). In the majority of natural infections, even with the more virulent members of the group, few or no clinical symptoms are present. However, clinical syndromes may occur, including severe paralysis, aseptic meningitis, herpangina, pleurodynia, myocarditis, exanthem, coryza and a variety of other conditions. Different enteroviruses may produce some of the same clinical syndromes and conversely one enterovirus may cause different syndromes under differing circumstances. The various clinical syndromes associated with members of the enterovirus group are shown in Table I. Several excellent references may be consulted for a more detailed description of the clinical symptomology and laboratory diagnosis of enterovirus infections.<sup>3-8</sup>

*Evaluation of results:* Since infection with enteroviruses is usually subclinical and virus excretion may persist for a period of weeks after initial infection, isolation of an enterovirus from the alimentary tract cannot be considered positive proof of etiological association with the patient's disease. Virus isolations are more meaningful when correlated with a significant rise in specific antibody titer in paired serum collected from the patient during the acute and convalescent stages of the disease. When the virus is isolated from blood, spinal fluid or pathological tissues from patients with typical syndromes, its etiologic association with the disease is more certain. Also, the possibility of concurrent infection with other viral, bacterial or fungal agents should be considered. Caution should be observed in evaluating the significance of an enterovirus isolate and accompanying rise in antibody titer until laboratory, clinical and epidemiologic findings have been completed and correlated.

TABLE I  
DIAGNOSIS OF ENTEROVIRUS INFECTIONS

| VIRUSES                                   | ISOLATION<br>TEST SYSTEM         | SEROLOGIC TEST                                               | CLINICAL SYNDROME                                                                                                                                                                                                                                                                                       |
|-------------------------------------------|----------------------------------|--------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Polioviruses,<br>types 1-3                | Monkey kidney<br>tissue cultures | Neutralization<br>(tissue culture)                           | Paralysis<br>(Complete to slight<br>muscle weakness)                                                                                                                                                                                                                                                    |
|                                           | Human tissue<br>cultures         | Complement<br>fixation                                       | Aseptic meningitis<br>Undifferentiated<br>febrile illness                                                                                                                                                                                                                                               |
| Coxsackieviruses, group A,<br>types 1-24* | Suckling mice                    | Neutralization<br>(mice)                                     | Herpangina (types 2, 3, 4, 5,<br>6, 8, 10)                                                                                                                                                                                                                                                              |
|                                           | Human tissue<br>cultures         | Complement<br>fixation<br><br>Hemagglutination<br>inhibition | Aseptic meningitis<br>(types 2, 4, 7, 9, 10)<br>Paralysis (infrequently)<br>(types 7, 9)<br>Exanthem (types 9, 16)<br>"Common cold"<br>(types 21, 24)<br>Undifferentiated febrile<br>illness (all types)                                                                                                |
| Coxsackieviruses, group B,<br>types 1-6   | Monkey kidney<br>tissue cultures | Neutralization<br>(tissue culture)                           | Pleurodynia (types 1-5)<br>Aseptic meningitis<br>(types 1-6)                                                                                                                                                                                                                                            |
|                                           | Human tissue<br>cultures         | Complement<br>fixation<br><br>Hemagglutination<br>inhibition | Paralysis (infrequently)<br>(types 2-5)<br>Severe systemic infections<br>in infants, meningo-<br>encephalitis, and<br>myocarditis (types 1-5)<br>Pericarditis, myocarditis<br>(types 1-5)<br>Upper respiratory illness<br>and pneumonia (types 4, 5)<br>Undifferentiated febrile<br>illness, types 1-6) |
| Echoviruses,<br>types 1-32**              | Monkey kidney<br>tissue cultures | Neutralization<br>(tissue culture)                           | Aseptic meningitis (types 2, 3,<br>4, 5, 6, 7, 9, 11, 14, 16, 18,<br>21, 30, 31)                                                                                                                                                                                                                        |
|                                           | Human tissue<br>cultures         | Complement<br>fixation<br><br>Hemagglutination<br>inhibition | Paralysis (mild) (types 2, 4,<br>6, 9, 11, 16)<br>Exanthem (types 4, 6, 9, 16,<br>18)<br>Respiratory disease<br>(types 4, 8, 9, 11, 20, 25)<br>Diarrhea (not proven<br>conclusively)                                                                                                                    |

\* Type 23 was never formally accepted as a new type since it was found to be identical with the previously described echovirus 9.

\*\* Type 10 echovirus (reovirus) was excluded from the group when it was shown to be a larger RNA virus; echovirus 28 is now considered to be a rhinovirus.



Yearly Variation of Enterovirus Infections

Previous epidemiologic and clinical studies have shown that certain enterovirus serotypes may predominate in a given area for one or two years and then disappear as a significant cause of disease for an unpredictable period of time. A similar predominance of enterovirus serotypes has been observed in the Connecticut area. Table II shows the enterovirus types isolated each year from 1960 through 1965 at the Connecticut State Department of Health Virus Laboratory. Over 90 per cent of these viruses were isolated from hospitalized patients with clinical syndromes compatible with enterovirus infection. Also, significant increases or decreases in neutralizing antibody titers against the infecting viruses were demonstrated in paired serums from 98 of the 111 patients studied. Since isolation of coxsackie A viruses in suckling mice has not been done on a routine basis in our laboratory, results on this group of viruses are not available (with the exception of coxsackievirus A9 which can be isolated in monkey tissue cultures).

Among the 111 enteroviruses isolated over the six year period, 19 distinct serotypes were represented. These included polioviruses 1 and 3; coxsackieviruses B1, B2, B3, B4, B5, and A9; and echoviruses 2, 3, 4, 6, 8, 9, 11, 14, 17, 23, and 25. Although several types were encountered each year, there was a tendency for certain types to predominate over the others. The predominant types in 1960 were polioviruses 1 and 3, and coxsackieviruses B4 and B5. In 1961 the types isolated most frequently were coxsackieviruses B4 and B5. The predominant isolate in 1962 was echovirus 4 and less frequently isolated was coxsackievirus B2. The principal isolate in 1964 was coxsackievirus B4. A

scattering of echoviruses and coxsackieviruses was detected in 1963 and 1965 without any specific type predominating. Additional results (not included in this report) confirming the predominance of these enterovirus serotypes during the six year period were obtained in neutralization tests conducted on paired serums from patients from whom enteroviruses could not be isolated. A similar yearly variation in the prevalence of enterovirus serotypes has been recognized in the New Haven area during a four year period from 1961 through 1964.<sup>9</sup> The most reasonable explanation for the predominance of certain serotypes in a community is the coincidence of a susceptible population and the introduction of the infecting agents under conditions favorable to easy transmission.

It is also evident from Table II that certain enteroviruses may be prevalent for one or more years and then disappear for a period of years as a significant cause of disease. For instance, coxsackievirus B4 was present during 1960 and 1961, disappeared for two years, and then reappeared in 1964 and 1965. Coxsackievirus B5 was isolated during 1960 and 1961 and then was absent for the following four years. Echovirus 4 was active in 1961, 1962, and 1963 and then disappeared for the next two years. Since the incidence of infection with these agents in the general population of Connecticut is unknown, one can only speculate that the disappearance of an enterovirus serotype after a period of activity is due chiefly to a reduction of the number of susceptible individuals within the state. It is also possible that some enterovirus strains of low virulence remain endemic for a period within a given area without causing a major epidemic and then disappear due to unknown factors.

TABLE II  
YEARLY VARIATION OF ENTEROVIRUSES ISOLATED  
IN CONNECTICUT FROM 1960 THROUGH 1965

| YEAR    | NUMBER OF ENTEROVIRUS ISOLATES* |   |   |                |    |    |    |    |    |           |   |    |   |   |   |    |    |    |    |    |
|---------|---------------------------------|---|---|----------------|----|----|----|----|----|-----------|---|----|---|---|---|----|----|----|----|----|
|         | POLIOVIRUS                      |   |   | COXSACKIEVIRUS |    |    |    |    |    | ECHOVIRUS |   |    |   |   |   |    |    |    |    |    |
|         | 1                               | 2 | 3 | B1             | B2 | B3 | B4 | B5 | A9 | 2         | 3 | 4  | 6 | 8 | 9 | 11 | 14 | 17 | 23 | 25 |
| 1960    | 17                              |   | 2 |                |    | 2  | 6  | 4  | 1  |           |   |    |   |   |   |    |    |    |    |    |
| 1961    | 3                               |   |   |                | 1  | 1  | 8  | 15 |    |           |   | 3  | 1 |   |   |    |    |    |    |    |
| 1962    |                                 |   |   |                | 3  | 1  |    |    | 1  | 1         |   | 9  |   |   |   |    |    |    |    |    |
| 1963    |                                 |   |   |                |    | 1  |    |    | 2  |           |   | 2  |   |   | 2 | 1  | 1  |    |    |    |
| 1964    | 1                               |   |   | 2              | 2  |    | 4  |    | 1  |           | 1 |    | 2 | 2 |   |    |    |    | 1  |    |
| 1965    |                                 |   |   |                |    |    | 1  |    | 1  | 1         |   |    | 1 | 1 |   |    |    | 1  |    | 1  |
| 1960-65 | 21                              | 0 | 2 | 2              | 6  | 5  | 19 | 19 | 6  | 2         | 1 | 14 | 4 | 3 | 2 | 1  | 1  | 1  | 1  | 1  |

\* A total of 111 enteroviruses was isolated over the six year period. Polioviruses presumably derived from oral vaccine are not included.

The dramatic disappearance of polioviruses from the Connecticut scene as a result of immunization with Salk and Sabin poliovirus vaccines is clearly illustrated. A total of 19 polioviruses was isolated in 1960, three in 1961, and only one in the following four year period from 1962 through 1965. The resurgence of poliomyelitis in Connecticut probably can be prevented by (1) continued use of vaccination programs implemented to reach susceptible individuals (2) the use of seroepidemiologic surveillance studies designed to assess community antibody patterns and (3) the rapid isolation and identification of the responsible poliovirus serotype at the start of an outbreak so that community-wide vaccination programs may be instituted before a statewide epidemic develops. Work on all three of these preventive measures is in progress at the Connecticut State Department of Health.

Seasonal Distribution of Enterovirus Infections

The seasonal distribution of enteroviruses prevalent during a two year period from 1960 through 1961 in six cities within the United States has been investigated recently by Gelfand and his associates.<sup>10</sup> Approximately the same seasonal pattern of low-winter, high-summer rates was recognized in each of the cities. However, some differences were noted among the six cities in the total number of isolations and in the degree of seasonal change. There appeared to be three patterns of enterovirus isolation: one for the cities in the southern part of the country (Atlanta and Miami), one for the northern cities (Minneapolis, Buffalo

and Seattle), and a distinctive one for San Francisco. In the southern cities at least a few isolations were made almost continuously during the year and seasonal plateaus lasting three to four months occurred during the summer and fall. By contrast, in the northern cities no isolations were made during the late winter and early spring months and peaked seasonal curves instead of plateaus were produced in the summer and fall. The pattern of isolation in San Francisco differed from those of the other cities in that only a few viruses were recovered in any month, and the differences in recovery between summer and winter were very small.

The seasonal distribution of enteroviruses isolated in Connecticut from 1960 through 1965 is shown in Table III. The pattern most closely resembles that described above for the northern cities. Out of a total of 111 enteroviruses isolated over the six year period, 97 were recovered during July, August and September with a peak occurring in August. Eleven viruses were isolated during the months of June, October and November, and only three viruses were isolated during the winter and spring months. The seasonal pattern of enterovirus infections observed in this study is distinctly different from the seasonal distribution of respiratory virus infections described in an earlier paper on the prevalence and significance of respiratory viral diseases in Connecticut.<sup>11</sup> Respiratory viral infections usually first appear each year in the late fall, after the enteroviruses have practically disappeared, and are chiefly prevalent in the winter and early spring. Simple

TABLE III  
SEASONAL DISTRIBUTION OF ENTEROVIRUSES ISOLATED  
IN CONNECTICUT FROM 1960 THROUGH 1965

| MONTH     | NUMBER OF ENTEROVIRUS ISOLATES* |   |   |                |    |    |    |    |    |           |   |   |   |   |   |    |    |    |    |    | TOTAL |
|-----------|---------------------------------|---|---|----------------|----|----|----|----|----|-----------|---|---|---|---|---|----|----|----|----|----|-------|
|           | POLIOVIRUS                      |   |   | COXSACKIEVIRUS |    |    |    |    |    | ECHOVIRUS |   |   |   |   |   |    |    |    |    |    |       |
|           | 1                               | 2 | 3 | B1             | B2 | B3 | B4 | B5 | A9 | 2         | 3 | 4 | 6 | 8 | 9 | 11 | 14 | 17 | 23 | 25 |       |
| January   |                                 |   |   |                |    | 1  |    |    |    |           |   |   |   |   |   |    |    |    |    |    | 1     |
| February  |                                 |   |   |                |    |    |    |    |    |           |   |   |   |   |   |    |    |    |    |    |       |
| March     |                                 |   |   |                |    |    |    |    | 1  |           |   |   |   |   |   |    |    |    |    |    | 1     |
| April     |                                 |   |   |                |    |    |    |    |    |           |   |   |   |   |   |    |    |    |    |    |       |
| May       |                                 |   |   |                |    |    |    |    |    |           |   |   |   |   |   |    |    |    |    |    |       |
| June      | 1                               |   |   |                |    |    |    |    |    |           |   |   |   |   |   |    |    | 1  | 1  |    | 3     |
| July      | 4                               |   | 2 | 1              | 1  | 2  | 2  | 7  |    | 1         |   | 2 | 1 |   |   |    | 1  |    |    |    | 24    |
| August    | 8                               |   |   | 1              | 3  | 1  | 11 | 5  | 2  |           |   | 7 | 1 | 1 | 2 | 1  |    |    |    | 1  | 44    |
| September | 7                               |   |   |                | 1  | 1  | 4  | 6  | 2  | 1         |   | 4 | 1 | 2 |   |    |    |    |    |    | 29    |
| October   | 1                               |   |   |                | 1  |    | 1  | 1  |    |           |   | 1 | 1 |   |   |    |    |    |    |    | 6     |
| November  |                                 |   |   |                |    |    |    |    | 1  |           | 1 |   |   |   |   |    |    |    |    |    | 2     |
| December  |                                 |   |   |                |    |    | 1  |    |    |           |   |   |   |   |   |    |    |    |    |    | 1     |

\* A total of 111 enteroviruses was isolated over the six year period. Polioviruses presumably derived from oral vaccine are not included.



answers are not available for explaining the different seasonal patterns observed for the enterovirus and respirovirus groups, however, epidemiologic factors which may influence the seasonal prevalence of these infections are (1) the effect of environmental conditions on the physiologic resistance of populations and (2) the variation in social habits with the seasons.

### Clinical Diagnoses and Virologic Studies in Connecticut Patients

Representative clinical and laboratory findings in 20 patients contracting enterovirus infections in Connecticut during a six year period from 1960 through 1965 are presented in Table IV. Enteroviruses active in Connecticut during this period were associated with a wide spectrum of clinical conditions. Polioviruses isolated in our laboratory were responsible for syndromes ranging from aseptic meningitis to fatal bulbar poliomyelitis. Coxsackieviruses were associated with gastroenteritis, aseptic meningitis, orchitis, pleurodynia, myocarditis, nonspecific febrile illness and pericarditis. Echoviruses were associated with gastroenteritis, aseptic meningitis, meningoencephalitis and exanthem. The laboratory diagnosis in 18 of the 20 patients was based upon both virus isolation and demonstration of a significant rise in neutralizing antibody against the virus type causing infection.

In the two fatal cases, bulbar poliomyelitis and neonatal myocarditis, the laboratory diagnosis was based only upon virus isolation from postmortem tissue specimens since both patients expired before convalescent serums could be collected. In general, neutralizing antibody titers in the acute serums were either absent or at a low level while the titers in the convalescent serums were considerably elevated. The diagnosis was strengthened in these cases by negative results obtained in serologic tests for influenza A, influenza B, adenovirus, psittacosis, Q fever, primary atypical pneumonia, respiratory syncytial, eastern equine encephalitis, western equine encephalitis, St. Louis encephalitis, mumps, lymphocytic choriomeningitis, herpes simplex, rickettsialpox, Rocky Mountain spotted fever and typhus.

### Summary

During a six year period from 1960 through 1965, 111 enteroviruses were isolated at the Connecticut State Department of Health Virus Laboratory from patients with symptoms of enterovirus disease. The following 19 serotypes were represented: polioviruses 1, 3; coxsackieviruses B1, B2, B3, B4, B5, A9; and echoviruses 2, 3, 4, 6, 8, 9, 11, 14, 17, 23, 25. Diagnostic increases in neutralizing antibody against the serotype isolated were found in the majority of the patients. These enteroviruses were responsible for a wide spectrum of disease syndromes

TABLE IV  
CLINICAL DIAGNOSES AND VIROLOGIC STUDIES IN CONNECTICUT  
PATIENTS WITH ENTEROVIRUS INFECTIONS

| PATIENT |         | CLINICAL DIAGNOSIS           | SPECIMEN    | VIRUS ISOLATED    | RECIPROCAL OF NEUTRALIZING ANTIBODY TITER IN SERUM |              |
|---------|---------|------------------------------|-------------|-------------------|----------------------------------------------------|--------------|
| NUMBER  | AGE/SEX |                              |             |                   | ACUTE                                              | CONVALESCENT |
| 1       | 3Y/F    | Aseptic meningitis           | Feces       | Poliovirus 1      | 32                                                 | 128          |
| 2       | 27Y/F   | Bulbar poliomyelitis         | Spinal cord | Poliovirus 1      | Not done                                           | Not done     |
| 3       | 3M/M    | Gastroenteritis              | Feces       | Coxsackievirus B1 | <4                                                 | 64           |
| 4       | 7Y/F    | Aseptic meningitis           | Feces       | Coxsackievirus B2 | 4                                                  | 64           |
| 5       | 32Y/M   | Meningitis, orchitis         | Feces       | Coxsackievirus B2 | 4                                                  | 32           |
| 6       | 12Y/M   | Pleurodynia                  | Feces       | Coxsackievirus B3 | <4                                                 | 64           |
| 7       | 41Y/F   | Aseptic meningitis           | Feces       | Coxsackievirus B4 | 4                                                  | 256          |
| 8       | 25Y/M   | Myocarditis                  | Feces       | Coxsackievirus B4 | 4                                                  | 256          |
| 9       | 10D/M   | Neonatal myocarditis         | Brain, lung | Coxsackievirus B4 | Not done                                           | Not done     |
| 10      | 2Y/M    | Nonspecific febrile illness  | Feces       | Coxsackievirus B5 | 8                                                  | 128          |
| 11      | 22Y/F   | Pericarditis                 | Feces       | Coxsackievirus B5 | 4                                                  | 256          |
| 12      | 31Y/F   | Pleurodynia                  | Feces       | Coxsackievirus B5 | <4                                                 | 1024         |
| 13      | 12Y/M   | Aseptic meningitis           | Feces       | Coxsackievirus A9 | 4                                                  | 64           |
| 14      | 13Y/M   | Gastroenteritis              | Feces       | Echovirus 3       | <4                                                 | 16           |
| 15      | 6Y/M    | Encephalitis                 | Feces       | Echovirus 4       | <4                                                 | 8            |
| 16      | 7Y/F    | Aseptic meningitis           | Feces       | Echovirus 6       | 4                                                  | 32           |
| 17      | 13Y/M   | Meningoencephalitis          | Throat swab | Echovirus 8       | 4                                                  | 64           |
| 18      | 34Y/M   | Aseptic meningitis, exanthem | Feces       | Echovirus 9       | 4                                                  | 128          |
| 19      | 4Y/M    | Gastroenteritis              | Feces       | Echovirus 11      | <4                                                 | 8            |
| 20      | 3M/M    | Meningitis                   | Feces       | Echovirus 25      | <4                                                 | 8            |

including exanthem, aseptic meningitis, gastroenteritis, nonspecific febrile illness, orchitis, pleurodynia, myocarditis, pericarditis, encephalitis, meningoencephalitis, fatal neonatal myocarditis and fatal bulbar poliomyelitis.

Although several enterovirus serotypes were encountered each year in Connecticut, there was a tendency for certain types to predominate over the others. The predominant types recognized were (1) polioviruses 1 and 3, and coxsackieviruses B4 and B5 in 1960 (2) coxsackieviruses B4 and B5 in 1961 (3) echovirus 4 and coxsackievirus B2 in 1962 and (4) coxsackievirus B4 in 1964. A scattering of echoviruses and coxsackieviruses are detected in both 1963 and 1965 without any specific type predominating during these years.

Most of the enterovirus isolates were recovered during the summer and early fall. Out of the total 111 enteroviruses isolated, 97 were recovered during July, August and September with a peak occurring in August. Eleven viruses were isolated during the months of June, October and November, and only three viruses were isolated during the winter and spring months.

Recent information has been presented on the classification of enteroviruses, the laboratory diagnosis of enterovirus infections and the clinical syndromes associated with enterovirus serotypes.

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*Those who have dissected or inspected many bodies, have at least learned to doubt; when others, who are ignorant of anatomy and do not take the trouble to attend to it, are in no doubt at all.—Giovanni Battista Morgagni. De Sedibus et Causis Morborum, 1761.*



# Polymyalgia Rheumatica

Siegfried J. Kra, M.D.\*

■ Muscle pain with stiffness of the shoulder and hip girdle is a frequent complaint in middle-aged and elderly persons and may be the presenting symptom in a wide spectrum of diseases. The most commonly considered causes are: osteoarthritis of the cervical spine and shoulder, rheumatoid arthritis, and psychogenic rheumatism. Polymyalgia rheumatica rarely is included.

Polymyalgia rheumatica is a definite syndrome, characterized by muscle pain and stiffness, with systemic manifestations such as fever, anemia, weight loss, and a markedly elevated sedimentation rate. Various names have been suggested for this syndrome: anarthritic rheumatism and myalgic syndrome of the aged with systemic manifestations.<sup>1,2</sup>

Only two reports of this disease have appeared in American literature.<sup>3,4</sup> The syndrome was first described by Kersley in 1951.<sup>5</sup> The term, polymyalgia rheumatica, was suggested by Barber of Great Britain in 1957.<sup>6</sup> Other reports, from France and the Scandinavian countries, have appeared describing this syndrome.<sup>7,8</sup>

The purpose of my report is to draw attention to this new rheumatic syndrome, which as yet, is not widely recognized in this country. I have had the opportunity to observe three cases of this disease over a two-year period.

*Clinical Features:* The onset of this disease may be fairly acute, with pain and stiffness of the proximal muscle groups of the limbs and neck, sometimes preceded by fatigue, lassitude, and loss of appetite. Most patients are women between the ages of 40 and 60.

The muscles of the neck, both shoulder girdles, and the upper arms, specifically, the posterior muscles of the neck, trapezius, deltoid, and biceps, predominantly are affected in all stages. Lumbar, gluteal, hamstring, and bilateral quadriceps muscles also are involved in most cases.

The patient may complain of some stiffness on rising in the morning and inability to perform simple activities, such as combing hair or reaching up to a shelf. Movements of related joints may be painful. Pain and stiffness may be so marked that patients may become totally incapacitated when the disease is at its height. They may lose weight and be confined to bed. Progressive joint changes are not seen.

At the time of the patients' first visit to the physician, the physical examination may be entirely normal. There is no evidence of muscular atrophy, muscular pain, swelling, or effusion in any joints. The patients will point to a muscle when describing the pain, and not to the articulation. The disease may remain at this stage and have a spontaneous remission. A small percentage of patients will exhibit increasing systemic manifestations such as fever and weight loss, and mimic the signs of a malignancy.

None of the patients described had any evidence of joint involvement,<sup>9</sup> other than osteoarthritis as found commonly in this age group.

*Laboratory Investigations:* One of the most striking, characteristic features of the syndrome is a very high sedimentation rate, which may vary from 42-122 by the Westergren method. The sedimentation rate parallels the activity of the disease. Anemia may occur and is usually hypochromic, normocytic. The white blood count, as a rule, is normal. Tests for rheumatoid factor and lupus cell preparation are negative. Serum protein electrophoresis may reveal low albumin and diffusely elevated gamma globulin. The fibrinogen level may be elevated. Electromyography as well as skin and muscle biopsies are normal.<sup>10</sup> X-ray examinations of the joints may reveal osteoarthritic changes compatible with this age group.

Polymyalgia rheumatica is readily distinguished from polymyositis and other myopathies by normal serum glutamic-oxalacetic transaminase levels, creatinine excretion, normal electromyography, and muscle biopsy. (See Figure 1).

Rheumatoid arthritis is distinguished from polymyalgia rheumatica by the presence of joint involvement and the usual criteria for its diagnosis.<sup>11</sup>

The etiology of this condition remains obscure. Some Swedish investigators believe that polymyalgia rheumatica belongs to the group of diseases that have underlying histological lesions of giant cell arteritis.<sup>12</sup> These authors suggest that polymyalgia rheumatica and temporal arteritis merge into one another. Biopsy specimens from some patients with

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FIGURE 1  
DIFFERENTIAL DIAGNOSIS OF POLYMYALGIA RHEUMATICA

|                           | PAIN | STIFFNESS | WEAKNESS | LATEX  | ESR      | SGPT     | CBC    | EMG      | MUSCLE BIOPSY |
|---------------------------|------|-----------|----------|--------|----------|----------|--------|----------|---------------|
| Polymyalgia               | +++  | +++       | ++       | Normal | Elevated | Normal   | ±      | Normal   | Normal        |
| Polymyositis              | +++  | +++       | +++++    | +      | Elevated | Elevated | ±      | Positive | Positive      |
| Rheumatoid Arthritis      | +++  | +++       | +        | +++    | Elevated | Normal   | ±      | Normal   | ±             |
| Peritendinitis Fibrositis | +++  | +++       | +        | Normal | Normal   | Normal   | Normal | Normal   | Normal        |

polymyalgia rheumatica showed some evidence of temporal artery involvement. However, temporal arteritis develops in much older age groups than does polymyalgia rheumatica.<sup>13</sup>

*Prognosis:* Patients usually respond dramatically to corticosteroids. If untreated, they may have a progressive downhill course, marked by inability to move any of their extremities because of severe pain. They become confined to their beds with generalized contracture and disuse atrophy developing. Some patients with no therapy at all experience a spontaneous remission. The end stage of untreated, progressive polymyalgia rheumatica cannot be confused with rheumatoid arthritis as in the latter there is evidence of joint involvement.

*Treatment:* Recovery is attained readily within a few weeks of treatment. Temperature returns to normal, and general well-being ensues. Generalized pain and stiffness disappear, and the sedimentation rate progressively drops.

The disease may last from 9 to 30 months. In every case a remarkable and rapid remission of symptoms was induced with adequate treatment. In some cases, pain and stiffness completely disappeared after 48 hours of corticosteroid therapy.

An initial dose of 30-40 mg of prednisone daily may be required to suppress pain and stiffness. It may be necessary to continue this dosage for 3 weeks or more, and then gradually taper the dosage over a 4-6 week period, until all symptoms have subsided.

The following program is usually successful: 40 mg of prednisone per day for the 1st 3 weeks; 30 mg per day the 4th week; 20 mg per day the 5th week; 15 mg per day the 6th week; 10 mg per day the 7th week; 5 mg per day the final week. Relapses may sometimes occur within the ensuing 2 years.

*Conclusion:* Polymyalgia rheumatica is a specific entity with characteristic symptoms of muscular pain, weakness and stiffness, a markedly elevated sedimentation rate sometimes associated with giant cell arteritis.

## Sample Case Histories

Case #1: A 78-year-old female suddenly felt pain and stiffness in the left shoulder and hip girdle. Fatigue and loss of weight were noted. Sedimentation rate was 55 mm per hour. There were mixed osteoarthritic changes in her shoulders and knees. Findings of enzyme studies were normal, as well as the rheumatoid factor and muscle biopsy. Thirty mg of prednisone was given for 20 days by which time the patient became asymptomatic.

Case #2: A 32-year-old male who was in good health, experienced pain and stiffness in the shoulder girdle, with severe pain in both knees and the quadriceps muscles. Nocturnal, throbbing headaches also developed. Physical examination was negative, except for some pain on moving the shoulder, neck, and thigh muscles. X-ray examination of the shoulder girdle showed osteoarthritic changes. The sedimentation rate was 100 mm per hour. The following findings were normal: biopsy of the deltoid muscle and enzyme studies. Sixty mg of prednisone daily was prescribed. After 2 weeks the patient responded.

Case #3: A 52-year-old female had a sudden onset of pain and stiffness in the neck and shoulder. The symptoms were not relieved by aspirin. Physical examination showed inability to raise her arms above her head. No evidence of joint effusion was found. X-ray examinations of the shoulder girdle disclosed early osteoarthritic changes. Laboratory examinations disclosed a normal white blood count, differential, hemoglobin, Latex test, serum uric acid, LE prep, SGOT, LDH, EMG, and muscle biopsy. The sedimentation rate was 80 mm per hour (Westergren) and bone marrow examinations disclosed normal hematopoiesis.

The patient received 40 mg of prednisone daily for 10 days. The dosage was then reduced to 25 mg daily for 3 weeks. Progressive improvement ensued and the patient became asymptomatic.

## POLYMYALGIA RHEUMATICA

### SUMMARY OF CLINICAL FINDINGS

|                              |                        |
|------------------------------|------------------------|
| Pain                         |                        |
| Stiffness                    | Proximal Muscle Groups |
| Fever                        |                        |
| Weight loss                  |                        |
| Anemia                       |                        |
| Elevated Sedimentation Rate  |                        |
| Normal EMG and Muscle Biopsy |                        |



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# Methoxyflurane Anesthesia For The Poor Risk Patient

Robert I. Schrier, M.D.

## Introduction

■ The management of poor risk patients who are to undergo surgery with anesthesia imposes limitations within which the physician-anesthetist must perform. Since physiological reserve may be considered a measure of operative risk, the patients we are concerned with in this discussion are deficient in one or more compensatory cardiovascular, pulmonary and renal mechanisms which constitute the physiological basis of reserve. In general, the degree of these deficiencies is inversely proportional to the tolerance poor risk patients have for surgery and anesthetics. This concept must influence our choice of the depressant anesthetic drugs available to anesthetize the poor risk patient.

Various technics deriving impetus from Artusio's work with "ether analgesia" have made possible the anesthetization of the critically ill.<sup>1</sup> The premise is based on two conditions:

(a) patients with already diminished compensatory mechanisms do not allow for additional physiologic trespass, and

(b) critically ill patients do not require the same levels of anesthetic depression necessary for the normal individual.

The lightest level of anesthesia which affords analgesia and amnesia to the patient and satisfactory operating conditions for the surgeon is the most desirable. The relative freedom of serious arrhythmias during light levels of anesthesia is also noteworthy.<sup>2</sup>

A second consideration in any anesthetic case management is the concomitant use of drugs such as norepinephrine, digitalis, epinephrine and isoproterenol, which, though necessary to bolster impaired cardiovascular activity, may in effect decrease it when used during the administration of many anesthetic agents.

The concentration of oxygen in the inspired anesthetic atmosphere must also be considered. Recent studies by Hallowell, Hedley-Whyte, and Laver at the Massachusetts General Hospital have confirmed our suspicions regarding the use of low potency anesthetics which must be administered in high concentration at the expense of oxygen.<sup>3</sup> Results based on patients undergoing mitral valvulotomy show that these individuals need more than 50 per cent oxygen in the inspired atmosphere

after thoracotomy was performed. Despite intermittent deep breaths shunting due to atelectasis was considerable and when nitrous oxide in fifty per cent concentrations was employed for anesthesia the resulting decrease in arterial  $pO_2$  was significant. This was promptly corrected by increasing the oxygen concentration to 99.5 per cent of the inspired anesthetic atmosphere.

To define further the indicated limitations in anesthetizing many poor risk patients one must mention the need for non-flammable anesthetics. The increased frequency with which electrical devices (i.e., cautery) are being used in the operating room limits the use of explosive anesthetics. It is not altogether unreasonable to predict that in the near future operating suites will no longer need to be electrically grounded. Considerable monetary expenditure could be curtailed in constructing the newer operating room facilities.

The criteria listed above for anesthetic management of the poor risk patient thus far include the following:

1. the ability to adjust easily concentrations of anesthetic so that while affording analgesia and amnesia suitable operating conditions can also be maintained.

2. the absence (or smallest incidence) of serious arrhythmias when catecholamines are also used.

3. the ability to employ maximum oxygen concentrations in the anesthetic atmosphere.

4. Non-explosive anesthetics.

The following case is representative of the above. An ever increasing number of similar anesthetic problems confronts us daily. While the management of each patient is of course distinct we can for discussion purposes consider their similarities.

## Case

The patient, a 43-year-old male, was admitted as an emergency from a veterans hospital. The tentative diagnosis of massive pulmonary embolism was confirmed by angiography in the X-ray Department and he was taken to the operating room for pulmonary embolectomy and inferior vena cava ligation.

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The patient's history revealed that he was convalescing subsequent to a myocardial infarction and cerebral vascular accident which had occurred one year prior to the present illness when suddenly he developed chest pain, elevated temperature and hemoptysis. The E.C.G. patterns were of right heart strain and a chest film showed left hilar prominence and increased heart size. The patient was started on heparin and transferred to our hospital seventy-two hours after the onset of symptoms.

On arrival in the operating room the blood pressure which had been 125/80 was down 15 mm Hg systolic. The pulse rate was 100 and the temperature 39°C. The patient was experiencing no pain and had been given atropine 0.5 mgm intramuscularly enroute to the operating room.

Examination of the eyes, ears, nose and throat was unremarkable. The neck veins were not distended and while the patient was breathing oxygen there was no evidence of cyanosis. The lungs were clear to auscultation and percussion and the heart sounds were distant with a marked increase in the second pulmonic sound. The hematocrit was 39, and W.B.C. 10,300. Because the patient's condition appeared to be deteriorating no additional studies were undertaken.

The findings of the angiocardiology were consistent with pulmonary artery thrombus or emboli occluding branches of the left pulmonary artery supplying the left lower lobe and partially occluding those of the left upper lobe. There was also extension of the occlusion across into the main and right pulmonary arteries.

Operative Course

Induction of anesthesia was accomplished with cyclopropane, closed circle mask, followed by methoxyflurane administered from a Pentec vaporizer. Because of the larger flows necessitated by this vaporizer, the anesthetic system was converted into a semi-closed one (Figure.)

The impaired pulmonary blood flow in this patient necessitated the use of a relatively rapid acting anesthetic during induction. For this reason, and also because of the release of catecholamines associated with its administration, cyclopropane is a choice agent for induction prior to methoxyflurane.

Intubation of the larynx was accomplished within seven minutes after the beginning of induction with the aid of 40 mgm I. V. succinylcholine. A #36 Murphy endotracheal catheter was inserted without difficulty.

The anesthetic concentration of methoxyflurane used during maintenance varied from 0.5 to 0.1 per cent as estimated from unpublished data by W. C. North. Oxygen mixtures administered from the anesthesia machine to the anesthesia circle ranged from 50 per cent during induction to 99 per cent during maintenance.

The patient's cardiovascular status began to deteriorate shortly after surgery was commenced and continued to do so, despite an epinephrine

drip (8 amps 1:1000 in 500 cc D & W) and Digoxin 1 mgm I.V., until he was placed on partial extracorporeal perfusion, Subsequently, after removing large clots from both pulmonary arteries, the patient's condition improved and a norepinephrine drip (4 amps/1000 cc) which was running very slowly after perfusion was found to be unnecessary at the termination of surgery.

Post-Operative Course

The patient was transferred to the intensive care unit awake and with endotracheal catheter in place. Moderate bleeding from the lungs and tracheobronchial tree, a result no doubt of manipulation (milking the lungs free of emboli) caused difficulty in the early post-operative period. Ventilation was controlled with a Bird ventilator and blood gas determinations returned to normal values within seven hours.

The first pain medication was required two hours after arrival in the intensive care unit and demerol 10 mgm I.V. was given (Table.)

TABLE I  
BLOOD GAS DETERMINATIONS DURING PULMONARY  
EMBOLECTOMY AND POST OPERATIVELY

|                     |           |                    |             |
|---------------------|-----------|--------------------|-------------|
| pCO <sub>2</sub>    | 23.4      | 24.4               | 24.6        |
| pO <sub>2</sub>     | 506       | 74.7               | 250         |
| O <sub>2</sub> Sat. | 100%      | 94%                | 96%         |
| pH                  | 7.5       | 7.36               | 7.39        |
|                     | 6:15 P.M. | 7:45 P.M.          | 12:00 P.M.  |
|                     | During    | Controlled         | Spontaneous |
|                     | Perfusion | Ventilation        | Respiration |
|                     |           | 99% O <sub>2</sub> | 40%         |

The remainder of the patient's post-operative course was relatively uneventful. The major problems involved resolution of the lung infarction and regulation of digoxin dosage, both of which were accomplished during the first week.

He was discharged to the Veterans Hospital on the 17th post-operative day.

Discussion

From this case and others we find that methoxyflurane as an anesthetic for the poor risk patient fulfills many of the desirable criteria we have outlined. The low vapor pressure of the drug (25 mm Hg at 20°C) as well as its high lipoid solubility (oil/gas partition coefficient 825) make for slowness in its uptake and its distribution. This quality renders control of analgesic levels relatively simple since over-dosage is partially related to time. In addition, a slower induction may actually be beneficial to the poor risk patient by allowing more time for compensatory homeostatic mechanisms to act. This property has long been known for diethyl ether and accounts for its popularity in the critically ill.

DIAGNOSIS: **Massive Pulmonary Embolism**

PRE-OP. **Pulmonary Embolectomy; Inf.Vena Cava Ligation**

POST-OP.

OPERATION:

SURGEONS: -----

PREANESTHETIC MEDICATION: **Atropine 0.5 mgm**

TIME: **4:30 PM**

EFFECT: **adeq.**

AGE: **43**

SEX: **M**

WT: **184lbs.**

BP: **125 / 80**

HGB: **Hct 39**

HABITUS: **obese**

TEETH: **no dentures**

EVALUATION: **poor risk**  
**myocardial infarct '63**  
**c.v.a. '63**  
**cardiovasc.collapse**  
**3 days ago**  
**on heparin**  
**E.K.G.Rt.HT.strain**  
**P.S. 1-2-3-4-5-E**

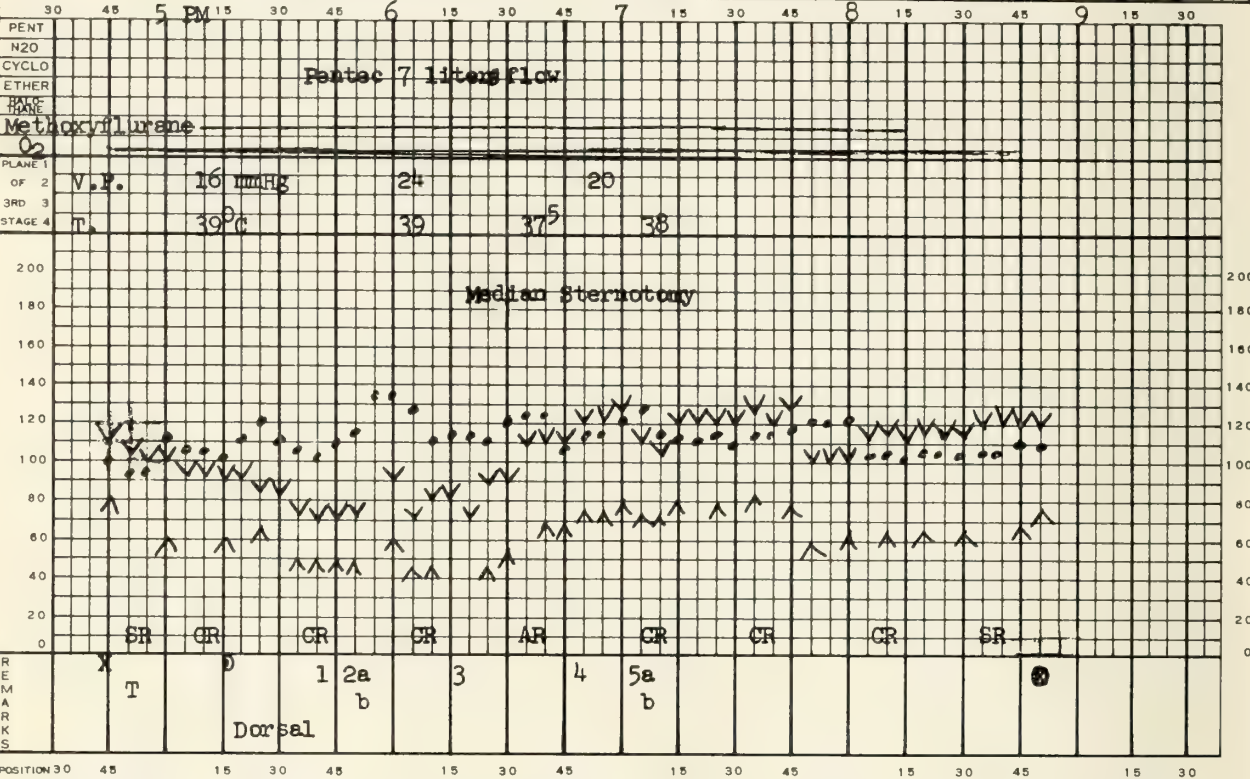


Fig.



Recent work by Ngai, Hanks, and Marnie, indicates that spinal reflex activity with methoxyflurane is obtunded before cephalic reflex activity and accounts for the profound muscle relaxation seen with this drug. Even in light levels of methoxyflurane this tendency towards good relaxation is evident.<sup>4</sup>

The relative stability of cardiac rate during methoxyflurane anesthesia has been clinically noteworthy and though arrhythmias have been seen with this agent their incidence appears to be low. The use of concomitant catecholamine drugs intravenously is potentially dangerous with any of the anesthetic agents; however, to date we have not experienced clinical difficulties with methoxyflurane under these circumstances.<sup>5, 6</sup>

The post-anesthetic patient who has had methoxyflurane is calm, analgesic, and if emesis occurs this is rarely remembered. The patient must be encouraged, however, to take intermittent deep breaths to avoid the possibility of atelectasis.<sup>7</sup> Used

judiciously, methoxyflurane proves to be a valuable addition to the pharmacologic management of poor risk patients.

### References

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5. Matteo, R., et al.: The injection of epinephrine during general anesthesia. *Anesthesiology*, 23: 360 1962-597, 1962; 24: 327, 1962.
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### PHYSICIAN-PATIENT RAPPORT

Never mistake common sense and tact for dishonesty and deceit, but always remember the possible dire consequences of showing the pity which you may feel for an incurably ill patient, and the tragedy that may result if he, rather than a responsible member of his immediate family, is frankly told the truth when hope alone may be the feeble flicker that sustains life.—H. U. Hopkins, M.D., Ed., *Leopold's Principles and Methods of Physical Diagnosis, Third Edition*. 1965, p. 2.

# THE PRESIDENT'S PAGE

## Title XIX in Connecticut

**T**ITLE XIX of Public Law 89-97, commonly designated as Medicaid, authorizes the appropriation of Federal funds, to be allocated to States on a supplementing basis of 50 to 83 per cent, to cover the expense of "care and services on behalf of families with dependent children under the age of 21, aged, blind or disabled individuals whose resources are insufficient to meet the costs of medical services, and for rehabilitation services to help such families attain capability for independence or self-care . . . ". In brief, the services to such individuals, for which payment is provided by state and federal revenues, includes (1) in-patient and out-patient hospital services, (2) other laboratory and X-ray services, (3) skilled nursing home services for those over 21, (4) physician services in an office, home, hospital or nursing facility, (5) home health care, (6) private duty nursing, (7) clinic services, (8) dental services, (9) physical therapy, drugs, dentures, eye-glasses, etc.

It is obvious that this portion of the Medicare Law has far-reaching implications for all components of the medical profession. Hospitals, clinics and other health care facilities, active practitioners of medicine and nursing, and those engaged in medical education will be affected. Unquestionably, changes in pattern of distribution, and demands for health care of patients, may be anticipated. Provision of adequate medical and nursing manpower to maintain present high standards of care will pose a real problem.

More than 30 States have submitted plans to implement the Medicaid program in 1966. In these areas, proposed basic family income levels of eligibility for financial aid will vary from \$2500 to more than \$6000. It is estimated that under these conditions full coverage of medical costs will thus be available for 40 percent or more of the population in some States. It has been stated that in New York State the Medicare-Medicaid programs may apply to nearly 80 percent of its citizens.

The program for Connecticut will be submitted to the legislature for approval soon after it convenes in January 1967. Committees of the Connecticut State Medical Society, and others, have been directing attention to the possible content of such proposed measures as they will affect practicing physicians.

It is very important for all members of the medical profession in Connecticut to familiarize themselves with the diverse aspects of Title XIX and assist in molding proposed legislation into a form reasonable and equitable to all concerned *before* it has been adopted. Medicine can serve the public interest by lending its advice and making its voice heard among our elected legislators.

ORVAN W. HESS, M.D.



# FROM THE GENERAL MANAGER'S OFFICE

WILLIAM R. RICHARDS, M.D., *General Manager*

Peter F. Villano

*Director of Public Relations*

160 St. Ronan Street, New Haven, Conn.

Telephone 865 0587

Josephine P. Lindquist

*Assistant to General Manager*

## SUMMARY OF ACTIONS

### COUNCIL MEETING

Thursday, November 17, 1966

#### I. Attendance

Present in addition to the Chairman, Dr. S. J. Martin, were: Drs. Hess, Bradley, Goldberg, Brandon, H. Caplan, Weise, Sr., Polivy, Rogol, Grendon, Egan, Abbot, Spitz, Shepard, Ayres, Nolan, Cramer, Fabro, Grant, Petrie, Pelz, Wilson and Roch. Also present: Mrs. Lindquist, Mr. Villano, Mr. Chilcoat (AMA) and Dr. Richards. Absent were: Drs. Gardner, W. Martin, M. Caplan, Hastings, Ciccarelli and Palomba.

#### In Memoriam

The Chairman informed the members of the Council that Morris P. Pitock, Bridgeport, a distinguished practitioner, medical leader, and past president of the Society had died on November 17, after a short illness. All members rose and observed a period of silent prayer in his memory. Thereafter, it was VOTED to instruct the General Manager to write a note of sympathy to Dr. Pitock's widow and family.

#### II. Routine Business

##### Approval Of Minutes

It was VOTED to approve the minutes of the meeting of October 12, 1966, as printed and distributed with the agenda.

##### Life Membership

It was VOTED to approve an application for Life Membership received from the following Active Member of the Society:

Albert F. Seibert, Hartford (HCMA)—1967

##### Election Of Student Members

It was VOTED to approve applications for Student Membership received from 11 residents of Connecticut who are enrolled in medical schools in the United States. A list of those elected will be published in the Journal.

##### Appointment—Delegates To Connecticut Advisory School Health Council

At the request of the CASHC, it was VOTED to appoint two delegates, for two-year terms, to the CASHC as follows:

Joseph J. Bellizzi, Hartford, Delegate

Louis A. Parrella, North Haven, Alternate Delegate

#### Date Of Next Meeting

The next meeting will be called for December 8, 1966 (preceding the semi-annual meeting of the House of Delegates), starting at 10:30 A.M.

#### III. Old, New And Special Business

##### Report—Congress Of County Medical Societies

E. Tremain Bradley, President-Elect, reported briefly on the history, organization, purposes and functions of the CCMS, and also on the proceedings of a recent regional meeting of the organization held in New York City. It was VOTED to receive Dr. Bradley's report as information.

Subsequently, Dr. Bradley introduced a series of four resolutions, three to be sent on to the AMA House of Delegates meeting in Las Vegas, and one to be presented to the CSMS House of Delegates on December 8, 1966. It was VOTED to adopt three of the four resolutions submitted by the President-Elect as follows:

##### (a) To AMA House of Delegates

SUBJECT: RULE FOR THE ELECTION OF MEMBERS OF AMA BOARD OF TRUSTEES

WHEREAS: By tradition, it has been a rule of the AMA House of Delegates that nominees for membership on the AMA Board of Trustees shall run for specific seats on the Board, rather than at large; and

WHEREAS: Such rule tends to deprive Delegates to the AMA of completely free choice in the election of members of the Board of Trustees; therefore be it

RESOLVED: That the House of Delegates of the American Medical Association adopt the rule that all nominees for membership on the AMA Board of Trustees shall run at large, and that those nominees receiving the most votes in relation to the number of seats open shall be declared elected.

##### (b) To AMA House of Delegates

SUBJECT: "CAMPAIGNING" BY NOMINEES FOR MAJOR OFFICES OF AMA

WHEREAS: By established custom, most candidates for major office and for membership on the Board of Trustees of the American Medical Association meet privately with selected groups of Delegates to inform those groups of their general position on important medical issues of the day; and

WHEREAS: Such "campaigning" serves an admirable purpose in allowing selected groups of Delegates to become acquainted with the candidates personally and to become informed as to their general positions on important medical issues; and

WHEREAS: It would be to the advantage of all Delegates to have an opportunity to so meet the candidates and to hear their personal views prior to the holding of elections; therefore be it.

RESOLVED: That, prior to the holding of elections, the House of Delegates of the American Medical Association grant each candidate for major office and for the Board of Trustees the courtesy of the floor for an appropriate period of time during which such candidates will be expected to state their general positions on important medical issues facing the Association and its members; and be it further

RESOLVED: That the House of Delegates invite all such candidates and/or those supporting them to make available to all Delegates biographical material on their personal and professional backgrounds.

(c) *To CSMS House of Delegates*

SUBJECT: STANDARDS OF ELIGIBILITY FOR  
MEDICAL ASSISTANCE

WHEREAS: The stated purpose of the Congress of the United States, in enacting Title XIX of P.L. 89-97, was to provide for the tax-supported financing of comprehensive, high quality medical services only for those persons found by the individual states to be totally indigent and/or "medically indigent"; and

WHEREAS: It is the responsibility of the legislatures of the individual states to establish standards of eligibility for entitlement to benefits under such Title XIX programs of Medical Assistance; and

WHEREAS: In several cases, state legislatures have imprudently established standards of eligibility at levels which entitle as much as 50 per cent of the general population (specifically, New York) to such benefits, with attendant incalculable but enormous costs to all taxpayers; and

WHEREAS: The Congress has already recognized its error in not placing limits on the standards of eligibility for Medical Assistance which the individual states may establish; therefore be it

RESOLVED: That the House of Delegates of the Connecticut State Medical Society urge the 1967 General Assembly, in enacting statutes to implement a Title XIX program of Medical Assistance in Connecticut, to seek to accomplish only what is intended by the Congress, and, thereby, to establish standards of eligibility for entitlement to benefits under the program which will reflect humani-

tarian but fiscally prudent definitions of indigency and "medical indigency" in this State; and be it further

RESOLVED: That the House of Delegates direct the Council to undertake effective legislative activities toward this end at the next session of the General Assembly.

**Report—Representative To 3rd National Congress  
On Medical Quackery**

It was VOTED to accept, with commendation, a report on the proceedings of this Congress by Max Caplan, Meriden, who attended it as a representative of the Society. It was further VOTED to ask Dr. Caplan, in consultation with the Editor, to prepare his report for publication in the Journal.

**Report—Ad Hoc Committee On Administrative  
Organization And Planning**

The Ad Hoc Committee filed a report with the Council on matters previously referred to it for study and recommendations. These were acted on as follows:

(a) *The Journal*: It was VOTED to accept the recommendation of the Ad Hoc Committee that the Journal be published in 1967 as it has been in prior years. The basis for this recommendation was that, while a substantial excess of expense over income is again anticipated in 1967, the encouraging increase in income from advertising realized this year will probably continue and, thereby, keep the deficit within reasonable limits.

(b) *Contract for the Assistant to the General Manager*: Having determined from Mrs. Lindquist that she is agreeable to placing herself under contract with the Society, it was VOTED to accept the recommendation of the Ad Hoc Committee that this be consummated, and it was further VOTED to approve the form of the contract recommended by the Committee. The initial contract will become effective on January 1, 1967, and will be for a period of five years.

(c) *Insurance Plans for CSMS Employees*: It was VOTED to accept the recommendation of the Ad Hoc Committee that individual Major Medical Plans and Health and Accident (Income Protection) Plans be furnished to all employees, with the Society paying the required premiums for individual coverage. Supplementing the basic Blue Cross and Blue Shield policies already in effect, the added cost to the Society will be \$860 annually. This recommendation was made in order to update the Society's employees insurance program in keeping with current business practice.

**1967 Budget—Report Of The Council's Fiscal  
Advisory Committee**

Having studied the 1967 Budget prepared and submitted by the FAC, it was VOTED to approve



the Budget, as submitted, and the Committee's recommendation that membership dues remain at the present level of \$50. The Budget, as approved, will be transmitted to the next meeting of the House of Delegates with the recommendation that it be approved by the House.

**Proposed Resolution Re Title XIX (Medicaid) Implementation**

It was VOTED to adopt a resolution on legislative action to introduce a bill at the 1967 General Assembly prohibiting any State officer, employee, or others from exercising control over, and/or interfering with, the practice of medicine or the manner in which medical services are customarily provided, such prohibition to be embodied in the statutes enacted by the Assembly to implement a Title XIX program of Medical Assistance in Connecticut. The resolution will be transmitted to the CSMS House of Delegates on December 8, 1966, with the Council's recommendation that it be adopted by the House.

**Report—Chairman Of Committee On Aging**

Kurt Pelz, Chairman of the Committee, filed a report with the Council on certain difficulties which had been encountered with representatives of the State Health Department with respect to the plan developed by the Committee, in consultation with the Connecticut Extended-Care Facilities Association, to help extended-care facilities obtain qualified physicians to serve on their Utilization Review Committees, as required by Part A of Title XVIII of P.L. 89-97. The difficulties encountered relate to certain recommendations of the Health Department (made subsequent to the Council's approval of the Committee's plan) which might invalidate or be in conflict with portions of the "Suggested Guide" developed by the Committee. It was VOTED to adopt Dr. Pelz's report, with commendation, and accept his recommendation that the "Suggested Guide" be mailed out to county associations and city societies, as approved on October 12, 1966, and that the Committee on Aging proceed to implement its plan to assist extended-care facilities, on request, to obtain physicians to serve on their utilization review committees.

**Report—CSMS Committee On Aging**

Having been asked by the Council to study and report on the feasibility of preparing a list of Connecticut physicians especially qualified in the field of geriatrics, a request for same having been previously received from the Commission on Services for Elderly Persons (via Commissioner of Health, Franklin M. Foote), the Committee submitted the following opinion:

"Inasmuch as medical care of the elderly may require the services of physicians in all branches

of medicine except pediatrics, the Committee feels that all physicians licensed to practice medicine by the State of Connecticut are qualified, in their areas of interest, to treat the elderly."

It was VOTED to adopt the opinion rendered by the Committee; to inform Dr. Foote of its adoption; and to send informational copies of the opinion to the component county medical associations.

**Report—Delegate To The Council Of New England State Medical Societies**

It was VOTED to accept, with thanks, the report filed by Ralph L. Gilman, Storrs, on his attendance at the Annual Meeting of the CNESMS, Boston, November 9, 1966, as one of the three Delegates to that organization from the Society. In particular, Dr. Gilman reported on adoption of revised by-laws by the CNESMS, which, while not embodying every recommendation made by the CSMS Council (October 17, 1966), he felt could easily be approved by the Society, with confidence.

It was further VOTED to approve the revised CNESMS bylaws (as reported by Dr. Gilman), in principle, but to request receipt of enough copies of the bylaws to enable each member of the CSMS Council to study same prior to taking definitive action, and, ultimately, submitting the bylaws to the CSMS House of Delegates for final approval.

**Report—Committee On Public Health**

Reporting on a possible problem which has arisen as a consequence of out-of-state laboratories soliciting contractual arrangements with Connecticut physicians to do all their laboratory work on a flat monthly payment basis, the Committee offered three recommendations to the Council:

(a) That (the ethics of) this matter be considered by the CSMS Council. It was VOTED to refer this recommendation to the Council's Committee on Preliminary Study of Censorship Questions for study and report. It was further VOTED to request the Section on Pathology to file with the Council an evaluation of these out-of-state laboratory operations from the standpoint of Connecticut pathologists.

(b) That the Council request the United States Public Health Service to investigate and make regulations so that the quality of laboratories crossing state lines meets the approval of USPHS; and

(c) That the Council request the State Department of Health to, to the best of its ability, evaluate the methods used by these out-of-state laboratories as to whether they meet or do not meet the standards required of laboratories in Connecticut, and, when the evaluation is completed, make the results available to all Connecticut physicians.

It was VOTED to approve recommendations (b) and (c), and to implement same.

**Report—Ad Hoc Committee To Study Liaison With Health Organizations**

Hilliard Spitz, Chairman of this Ad Hoc Committee, filed a report which stated that other health organizations (in particular, the Connecticut Nurses Association and the Connecticut Pharmaceutical Association) had expressed substantial interest in forming such a liaison group within which they could discuss freely professional and socioeconomic problems of common interest. The report proposed that the Society take the initial steps necessary to form the liaison body, but that, once established, it should operate autonomously with continuing representation, but not direction, from the Society. It was VOTED to accept the report, and to direct the Chairman of the Council to appoint a CSMS committee to act as the nucleus for the formation of such a liaison group, and to take the necessary steps to enlist the participation of interested health organizations, starting with the CNA and the CPA.

**Request For Support—Connecticut Pharmaceutical Association**

The Executive Committee of the CPA has urged the National Association of Retail Druggists and the American Pharmaceutical Association to seek changes in the Harrison Narcotics Act (at Federal level) which would permit the prescribing of Class A narcotics by licensed physicians via the telephone and the pharmacist to honor such unwritten prescriptions. The CPA's Executive Committee urged the Council to seek to enlist the support of the American Medical Association in this national legislative undertaking, and suggested that, if it approved the purpose of the project, the Council might introduce a pertinent resolution on same at the next meeting of the AMA House of Delegates at Las Vegas.

It was VOTED to approve the purpose of the proposal made by the CPA's Executive Committee, and to instruct the Connecticut Delegation to introduce the following resolution at the Las Vegas meeting of the AMA House of Delegates:

*To AMA House of Delegates*

SUBJECT: TELEPHONE PRESCRIBING OF  
CLASS A NARCOTICS

WHEREAS: In certain emergency situations, the patient will be greatly benefitted if the pharmacist may legally dispense Class A narcotics on the telephoned prescription order of the physician; and

WHEREAS: The Harrison Narcotics Act presently prohibits the pharmacist from honoring a telephoned prescription for Class A narcotics; and

WHEREAS: The National Association of Retail

Druggists and the American Pharmaceutical Association are being urged to seek legislative changes at the Federal level which would permit such prescribing by telephone, therefore be it.

RESOLVED: That the House of Delegates of the American Medical Association direct the AMA Board of Trustees to communicate with the National Association of Retail Druggists and the American Pharmaceutical Association with a view toward working jointly with those organizations to effect legislative changes in the Harrison Narcotics Act at Federal level which would permit the pharmacist, in his discretion, to honor a physician's telephone order for Class A narcotics, with provision made that the prescribing physician must supply the dispensing pharmacist with a written prescription within a specified period of time.

**Appointment—Ad Hoc Committee To Study Paramedical Responsibility**

J. Alfred Fabro, Torrington, reported on discussions held recently in his community relative to the increasing problems posed by the modern "team" approach to the medical care of patients, particularly in regard to the ethical and legal implications involved when license registered nurses, practical nurses, medical technicians and others carry out procedures which, technically, constitute the practice of medicine. E. Tremain Bradley, President-Elect, informed the Council that he and the General Manager had been sitting in with representatives of the Connecticut Hospital Association, the Connecticut Nurses Association, and their attorneys, at joint discussions of these problems (particularly with respect to R.N.'s) from which it is hoped that a uniform set of guiding principles may be developed regarding such implications for the registered nurse.

Pursuant to these two reports, it was VOTED to direct the Chairman of the Council to appoint an ad hoc committee to study and report on all ethical and legal aspects of the participation of licensed registered nurses, practical nurses and other paramedical personnel in the medical care of patients, in consultation with the State Health Department, the Attorney General, and representatives of all paramedical groups concerned.

**Supplemental Agreements To The Dependents' Medical Care Program Contract**

The Council was informed that the Advisory Committee on Dependents' Medical Care Program has under study a supplemental agreement to the basic agreement now existing between ODMC and the Society. Taking no position on the merits of the supplemental agreement in question, the Council VOTED to inform ODMC that the Society will be unable to consider approving any expansion or changes of the present program until ODMC has



presented to the Society its plan to embody in the basic agreement the CSMS policies regarding paying physicians their "usual and customary fees, as determined at local level" for services rendered to DMCP beneficiaries. Note was made that the 1965 basic agreement is under extension until February, 1967, for the purpose of giving ODMC time to prepare a new plan embodying CSMS policies, and the Society time to study and evaluate same.

N.B.: *The foregoing is a summary of the proceedings and actions of the Council on November 17, 1966. Detailed minutes of the meeting are on file at 160 St. Ronan Street, New Haven, for perusal by any interested member of the Society.*

**PLACEMENT OPPORTUNITIES**

**PSYCHIATRIST**—Full-time for small, but expanding psychiatric inpatient service in general hospital. Short-term therapy provided on open ward. Also, Mental Hygiene Clinic and Day Treatment Center on hospital grounds which offer continuity of care. There will be opportunities for teaching paramedical personnel and inservice programs. Salary dependent on qualifications. Excellent fringe benefits. Apply: Chief of Staff, VA Hospital, Newington, Connecticut 06111.

**CLINICAL PHARMACOLOGIST** — Physician who wants to combine medical knowledge, scientific inquisitiveness and administrative skills. Highly desirable are previous experience in pharmaceutical industry, background of private practice and some type of specialized medical training, although a strength in one area may outweigh a lack in others. As a member of Research Div., he will be active in planning new medicinal research programs. Between 10 percent and 20 percent of the time, he will be on scientific field trips or attending various professional meetings, but will rarely be gone more than 3 consecutive days. Members of Clinical Pharmacology Dept. are encouraged to publish scientific papers based on their own studies. Contact: D. V. Vines, Personnel Mgr., Chas. Pfizer & Co., Groton, Conn. 06430

**INTERNIST** — The Chapel Medical Group is looking for an internist. This is a three-man group and they have a regularly visiting specialist consultant staff with modern clinic facilities, with scheduled training and vacation periods. Starting salary is \$15,000-\$18,000, with a partnership in one year. Please submit qualifications to Chapel Medical Group, 1308 Chapel Street, New Haven, Conn. 06511

**PLACEMENT WANTED**

**PEDIATRICIAN** — 37 year old Board eligible pediatrician with background in general pediatrics

and pediatric oncology desires to associate with other Pediatricians in New Haven area. Military obligations completed, applied for Connecticut license.

**OBS-GYN**—Board eligible, 31 years old, seeks association leading to partnership. Will complete military obligations February 28, 1967. Had 4 years residency, fully trained.

**1967 MEETINGS**

- January 17-19**—New England Postgraduate Assembly will be held at the Statler-Hilton Hotel, Boston, Massachusetts. Advance programs will be mailed shortly.
- April 12-13**—Seminar on Hospital Infections in Connecticut to be sponsored by Connecticut State Medical Society, Connecticut Hospital Association, Yale University School of Medicine, Connecticut State Department of Health and the Communicable Disease Center of the Public Health Service.
- April 25-27**—175th Annual Meeting of the Connecticut State Medical Society to be held at the Hartford-Hilton Hotel, Hartford, Connecticut.

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# Welcome, New Members . . .

## **Litchfield County Medical Association**

- Thomas H. Danaher, M.D., 379 Prospect Street, Torrington, Connecticut 06790.  
Ashbel G. Gulliver, Jr., M.D., 19 Taylor Street, Torrington, Connecticut 06790.  
Joseph P. Macary, M.D., Charlotte Hungerford Hospital, Torrington, Connecticut 06790.  
Duncan R. MacMaster, M.D., Charlotte Hungerford Hospital, Torrington, Connecticut 06700.  
Walter P. Reyelt, Jr., M.D. Sharon, Connecticut 06069.  
Reginald D. Smith, M.D., Charlotte Hungerford Hospital, Torrington, Connecticut 06790.  
Capt. Ronald J. Pimpinella, M.D., Martin Army Hospital, Fort Benning, Georgia.

## **New London County Medical Association**

- Mariano F. Songco, M.D., Norwich Hospital, Norwich, Connecticut 06360.

## **New Haven County Medical Association**

- Jerome T. Combs, M.D., 45 Fair Street, Wallingford, Connecticut 06492.  
William R. Coyle, III, M.D., 56 Minerva Street, Derby, Connecticut 06418.  
Alan J. Davidson, M.D., Yale-New Haven Hospital, New Haven, Connecticut 06504.  
Robert H. Fenton, M.D., 690 Howard Avenue, New Haven, Connecticut 06519.  
Louis J. Ferando, M.D., Hospital of St. Raphael, New Haven, Connecticut 06511.  
Amado F. Fernandez, M.D., Griffin Hospital, Derby, Connecticut 06418.  
Peter J. Fine, M.D., 2 Church Street South, New Haven, Connecticut 06519.  
David S. Fischer, M.D., 960 Main Street, Branford, Connecticut 06405.  
James I. Gilman, M.D., 789 Howard Avenue, New Haven, Connecticut 06504.  
Joseph L. Goodman, M.D., 219 West Main Street, Meriden, Connecticut 06450.  
Andrew J. Graham, M.D., 380 Boston Post Road, Orange, Connecticut 06477.  
Elliott M. Grau, M.D., 640 Chapel Street, New Haven, Connecticut 06511.  
Bernard B. Greenhouse, M.D., Yale Medical School, New Haven, Connecticut.  
Nabil I. Habib, M.D., 153 Main Street, Ansonia, Connecticut 06401.  
Robert Hook, M.D., 789 Howard Avenue, New Haven, Connecticut 06504.  
Peter R. Huttenlocker, M.D., Yale-New Haven Hospital, New Haven, Connecticut 06504.

- Lillian L. Imperi, M.D., 435 College Street, New Haven, Connecticut 06511.  
Gil G. Job, M.D., 140 Sherman Avenue, New Haven, Connecticut 06511.  
Foster Kay, M.D., 2447 Whitney Avenue, Hamden, Connecticut 06518.  
Kristaps J. Keggi, M.D., 333 Cedar Street, New Haven, Connecticut 06510.  
Gerald L. Klerman, M.D., 34 Park Street, New Haven, Connecticut 06519.  
Norman J. Marieb, M.D., 380 Boston Post Road, Orange, Connecticut 06477.  
William S. McClanahan, M.D., 477 South Broad Street, Meriden, Connecticut 06452.  
Giacomo Messore, M.D., Hospital of St. Raphael, New Haven, Connecticut 06511.  
Robert A. Nemiroff, M.D., 123 York Street, New Haven, Connecticut 06511.  
Michael F. Nezhad, M.D., 1389 W. Main Street, Waterbury, Connecticut 06708.  
John W. Paggioli, M.D., 199 W. Main Street, Meriden, Connecticut 06450.  
Jonathan H. Pincus, M.D., 333 Cedar Street, New Haven, Connecticut 06519.  
Walter M. Presnell, M.D., Undercliff Hospital, Meriden, Connecticut.  
Kyum S. Pyun, M.D., 181 Cook Avenue, Meriden, Connecticut 06450.  
Renato H. Rojas, M.D., 789 Howard Avenue, New Haven, Connecticut 06504.  
William Russell, M.D., 81 Carpenter Avenue, Meriden, Connecticut 06452.  
Brigid I. Russell, M.D., 81 Carpenter Avenue, Meriden, Connecticut 06452.  
Carl W. Scheer, M.D., 335 Cook Avenue, Meriden, Connecticut 06450.  
Lorraine D. Siggins, M.D., 435 College Street, New Haven, Connecticut 06520.  
Allen R. Traurig, M.D., 1389 West Main Street, Waterbury, Connecticut 06708.  
Alexander W. C. von Graevenitz, M.D., 789 Howard Avenue, New Haven, Connecticut 06504.

## **Tolland County Medical Association**

- Juan Mendoza, M.D., Johnson Memorial Hospital, Stafford Springs, Connecticut 06076.  
Michael R. Sharon, M.D., 57 Union Street, Rockville, Connecticut 06066.

## **Windham County Medical Association**

- George E. Becker, M.D. 132 Mansfield Avenue, Willimantic, Connecticut 06226.  
Seymour Manzoni, M.D., 459 Valley Street, Willimantic, Connecticut 06226.



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## Around The State

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### New Haven County

#### 183rd Semi-Annual Meeting

#### New Haven County Medical Association

October 27, 1966

The 183rd Semi-Annual Meeting of the New Haven County Medical Association was held Thursday, October 27, 1966 at the Waverly Inn in Cheshire, Connecticut.

The business meeting was called to order at 3:30 p.m. by the presiding officer, President Max Caplan who welcomed a large turnout of members and guests which included Doctors Orvan E. Hess, President of the Connecticut State Medical Society and E. Tremain Bradley, the President-elect. The speaker and vice-speaker of the House, Kenneth Brandon and Henry Caplan, respectively; William R. Richards, General Manager; the new Director of Public Relations, Peter Villano; Delegates from Hartford and Fairfield Counties, and Attorney John F. Cipriano, the President of the New Haven County Bar Association.

An excellent semi-annual report was offered by our councilor, Frank Abbot. A brief summation indicates he suggested that information for review by the council should be sent beforehand to the office of the general manager; the council found and moved that direct billing of the patient by the physician for services rendered under Part B of Medicare law is legal and ethical and the preferred method of re-imbursement for such services. He called to the attention of Connecticut General Insurance Co. that New Haven County does have a satisfactory Review Committee.

Dr. Abbot stated that for patients under Mr. Bernard Shapiro, Welfare Commissioner, the state would re-imburse physicians on the basis of the usual and customary fee for services rendered. He added, however, it remains to be seen what the next Legislature will do about this.

A motion was made and seconded to accept the Councilor's report with commendation. PASSED.

Other committee reports were presented and accepted as read, or previously filed.

The Clerk, reporting for the Board of Governors, informed the meeting that all meetings of the Board have been reported in *CONNECTICUT MEDICINE*. He also announced the distribution of the Budget for the coming year and asked its acceptance, which was moved. Dues will remain at the same figure.

Thirty-four candidates for election to provisional membership were presented and elected.

A Nominating Committee to work with the Board of Governors was elected as provided for in the By-Laws, and the meeting was closed on a very successful note, after setting the date for the 1967 184th Semi-Annual Meeting as October 26, 1967.

A social hour was followed by dinner at which the guest speaker was George E. Hall, J.D., Staff Associate, Law Department, A.M.A. His subject was "Current Legal Problems Facing Medicine."

Respectfully submitted,

H. A. LEVIN, M.D., Clerk

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## BOOKS RECEIVED

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*Books received for review are acknowledged in this department and such acknowledgement must be regarded as a sufficient return for the courtesy of the sender. Selection will be made for review in the interests of our readers and as space permits.*

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*Modern Home Remedies And How To Use Them.* Morris Fishbein, M.D. Doubleday & Co., Inc. New York, 1966. 129 pp. \$3.95.

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*Relationships: Hospitals And Hospital-Based-Specialists.* American Hospital Association, Chicago, Illinois, 1966. 34 pp. 75¢.

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*Clinical Management Of Behavior Disorders In Children.* Third Edition, Harry Bakwin, M.D. and Ruth Morris Bakwin, M.D., W. B. Saunders Company, Philadelphia and London, 1966. 652 pp. with illustrations. \$14.50.

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*A Manual of Tropical Medicine.* Fourth Edition, 323 illustrations, 8 in color, George W. Hunter, III, Ph.D., Col. U.S.A. (Ret.), William W. Frye, Ph.D., M.D., Sc.D. (Hon.) and J. Clyde Swartzwelder, Ph.D., W. B. Saunders Company, Philadelphia and London, 1966. 871 pp.

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## Doctor's Office

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Arthur Brovender, M.D., announces the removal of his office to 10 River Street, Norwalk.

Edward M. Keelan, M.D., announces the removal of his office from 32 Imperial Avenue to 136 Main Street, Westport.

Franklin F. Nejame, M.D., announces the opening of an office for the practice of obstetrics and gynecology at 331 Maple Avenue, Cheshire.

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## OBITUARIES

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### **Morris Philip Pitock, M.D.**

**1902 - 1966**

Sincere condolences are extended to the family of Dr. Morris P. Pitock whose unexpected demise occurred on November 17, 1966. Dr. Pitock had suffered a massive cerebral hemorrhage from which he never recovered. His distinguished career was highlighted by the many officer's positions he held in the various societies to which he belonged.



Born on August 6, 1902, in Philadelphia, Pennsylvania, he was graduated from Franklin and Marshall College with a B.A. degree in 1925 and a M.A. degree from the same scholastic institution in 1926. He earned his medical degree from Tufts College of Medicine in 1930. After completing an internship at Bridgeport Hospital in 1932, he practiced general medicine in Fairfield until 1938 when he confined his practice to obstetrics and gynecology. In 1947, he became a diplomate of the American Board of Obstetrics and Gynecology. His medical practice was interrupted from May, 1942 to December, 1945 when he served voluntarily in the U. S. Air Force in the North African theater as flight surgeon with the rank of major.

Dr. Pitock held memberships in the Bridgeport Medical Association, the Fairfield County Medical Association, the Connecticut State Medical Society,

the American Medical Association and the Connecticut Society of the American Board of Obstetrics and Gynecology. He was a founding Fellow of the American College of Obstetrics and Gynecology. He had served president's terms in both the county and state Medical Associations, and was advisor to the Women's Auxiliary to the Fairfield County Medical Association. He had been appointed recently alternate delegate to the American Medical Association. He was currently chairman of the Bridgeport Hospital Department of obstetrics and gynecology, the formulation of which he was directly responsible. Last spring, he was elected chairman of the Connecticut Conference of Hospital Chiefs of Staff for the federal program on heart disease, cancer and stroke. In 1964, he became chairman of the Executive Committee and Chief of Staff of Bridgeport Hospital. Dr. Pitock was also chairman of the Hospital Regional Planning Committee of the Greater Bridgeport Area. In recent years he was associated in his practice with the Obstetrics and Gynecology group.

He is survived by his charming wife, the former Dr. Marjorie Fulstow, former pathologist at Boston Psychopathic Hospital and cytologist at Bridgeport Hospital, his son, Timothy F. Pitock, his daughter, Mrs. George House, five grandchildren and a brother, David Pitock and several nieces and nephews.

Dr. Pitock's interests extended beyond the limits of medicine. He was an avid reader, a connoisseur of music and a skilled cabinet maker.

Dr. Pitock possessed a perceptive mind, a dauntless spirit and a keen wit. He was willing to assume leadership; he was dedicated to his profession. He was a man of purpose whose tireless efforts in the formation of medical policy at the local and state levels will have long lasting effects. We deeply regret that he will no longer be a part of future conclaves. The void created by his absence will be sorely felt by those of us who knew him personally, as patient, associate and friend. It would be difficult to measure the loss born by the Bridgeport Hospital community which he served so selflessly during his entire career.

GEORGE J. GEANURACOS, M.D.



## Samuel Philipson, M.D.

1896 - 1966

Dr. Samuel Philipson, a member of our medical community for forty-four years, ended his service to humanity on November 5, 1966.

Born in Ossining, New York, on November 8, 1896, he had nearly reached the biblical three score and ten. His preliminary education was completed in his home community, and he entered the New York Medical College in 1914, receiving his degree in medicine in 1918. He served his internships in



the New York area at the Harbor Hospital, and the Metropolitan Hospital. He took a course at the New York Lying-In Hospital, preparing himself for the practice of obstetrics. He was married in 1920 to Edith Alderman of this city, and entered practice in New Haven in 1922.

Dr. Philipson was a diligent, meticulous practitioner, unsparing of himself, and especially watchful of the welfare of his patients at all times. In later years of his career, he discontinued the practice of obstetrics and concentrated his activities to metabolic problems, as related to obesity. He was forced to limit his practice in more recent years after the onset of his coronary disease. He was at his office only a few days before entering Yale-New Haven Hospital for his final days. His survivors are his wife, his sons, Davis of Woodbridge, Dr. Morris, who is the director of the Chicago University Press, and Robert of Washington, D. C., three brothers and three sisters. Other than these, he lives in the memories of his community, his colleagues, and a host of grateful patients and their families. He was an active member and participant of the local County and State Medical Societies,

of the New Haven Medical Society, local, County and State Medical Societies, and a past-president of the New Haven Obstetrical Society.

All who knew him will miss his friendliness and his counsel.

MAXWELL LEAR, M.D.

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## In Memoriam

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**Kartin, Bernard L.** — New Haven; Columbia University School of Medicine, 1939. Dr. Kartin was an internist in New Haven for over 20 years. He was an assistant clinical professor of medicine at the Yale School of Medicine. He was a member of the New Haven County Medical Association, the Connecticut State Medical Society, the American Medical Association, and the American Board of Internal Medicine. Dr. Kartin died October 16, at the age of 54.

**Reich, Upton S.** — Trumbull; University of Virginia Medical School, 1909. Dr. Reich was a general practitioner in the Bridgeport area for over 40 years. He was on the consulting staff of the Bridgeport Hospital. He was a member of the Fairfield County Medical Association, the Connecticut State Medical Society, and the American Medical Association. Dr. Reich died July 8, at the age of 78.

**Spiegel, Charles M.** — New Haven; Hahnemann Medical College, 1936. Dr. Spiegel was a general practitioner in New Haven for over 20 years. He was a member of the New Haven County Medical Association, the Connecticut State Medical Society, and the American Medical Association. Dr. Spiegel died November 3, at the age of 56.

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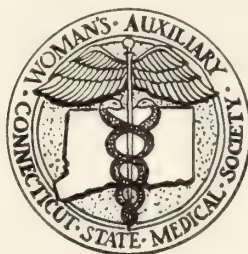
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The Woman's Auxiliary to the Connecticut State Medical Society held their semi-annual meeting on November 15, 1966 at the Park Plaza Hotel in New Haven, Conn. President, Mrs. John D. O'Connell, presided. The Doctors Orvan W. Hess, President; Waldo E. Martin, Secretary; William R. Richards, General Manager, attended. Mr. Matthew Barbieri, Director, Department of Physical and Health Education, Hamden Schools spoke on "A School Health Program, its Progress and Problems."

The following report was given by Mrs. Anthony P. Cipriano, president-elect, on the 23rd Annual Conference of State presidents and presidents-elect in Chicago.

## **Annual Report Of The President-Elect**

The 23rd Conference of the Woman's Auxiliary to the American Medical Association was held October 2-4 in Chicago. Your president and president-elect attended along with Betty Gardner who is a director on the national board as well as serving on state board.

As usual much was discussed and learned. I especially enjoyed the informal meetings and discussions which seem to bring everyone to speak our thoughts more freely, thus a better exchange of ideas which we all hope for. In this way we learn from each and also it gives the national board a better idea of how to plan the year by adding to or discarding projects depending on acceptance and response of the States. Two such meetings were, one on our arrival Sunday night at the Eastern Regional Dinner where we sat with the president and president-elect of Maine and also the Editor of *MD's Wife*. It was here that President Hudson of the A.M.A. spoke briefly on "Medicare." The other informal meeting was with president-elect Ritter. An open discussion was on programming and membership.

Heading the morning program was a discussion of Title 19, the implementation of Title 18, "Medicare" by Ellen Winston, Ph.D., Commissioner, Welfare Administration, HEW who described the bill; Howard Hassard, Executive Director, California Medical Association and Dr. Henry Finberg, Executive Vice President of the New York Medical Society, both pointed out that Title 19 can be a blessing or a calamity, depending on the wisdom of the States' legislators who will implement the program. "A.M.A. supports the concept of the program, we are, however concerned about the extensive benefits offered, with no co-insurance, no deductibles and no age-factor," he said. He then suggested the following amendments, to provide: 1. Direct payment to the patient; 2. Free choice of physician; 3. Reimbursement on usual and customary charges; 4. Use of insurance carriers in implementing payment; 5. That the federal contribution shall not be affected by the identity of the agency which insures the expense; 6. State plans to vary, within the state, standards of eligibility; and 7. Advisory council, including physicians.

Dean W. Roberts, M.D., Executive Director, National Commission on Community Health Service, then spoke on "Health is a Community Affair," pointing out that communities have not kept pace with the increased complexities of health services.

At lunch, Monday, Patricia Lanier, M.D. vice-president, NEC Region, American Association of University Women, urged the auxiliary to be women of action, to be individuals rather than develop an image, assume the role of leadership and in leadership to use brains, not emotion!

In the afternoon we heard Mrs. A. C. Mills, Director, American Red Cross, who told us the Red Cross's responsibility is to the individual during the disaster and their return to normal. Mrs. J. S. Van Wort, Mid-west regional chairman, American Farm Bureau—we found their group not un-



like ours in their ideals and their problems. Mrs. J. A. Campbell, Chairman, Education Fund, League of Women Voters reminded us that "women should learn political skills for today all levels of government are active in all phases of life." This completed the sessions for Monday.

Mrs. Frieda Engel, Jane Addams Graduate School of Social Work, University of Illinois, urged us not only to continue our efforts in the home-maker services, but to double them.

Mrs. Floyd Anderson, Chairman, Meals on Wheels Committee, presented a slide program on the San Francisco Auxiliary's Meals on Wheels project, describing its operation. They service about forty people three times a week. The preparation is done by volunteers with only two part-time paid workers in the kitchen of the auxiliary's building.

The conference was honored to have as the Tuesday Luncheon speaker, His Excellency, Vu Van Thai, Ambassador of Vietnam, Washington, D. C. It was quite evident that we were all moved when he spoke of the health problems in Vietnam. He said, "Vietnam is virtually a reservoir of every disease known to man. He also told us that American contribution in medical supplies and teams have been treating an average of 40,000 a month and that 13 million have been vaccinated against cholera, plague, and polio in the first six months of this year. The Ambassador finished by saying, "The American people are willing to accept that their feelings are as necessary as their might to make of the earth a liveable place—they believe that technical progress belongs to the entire mankind, and they try to sooth the drama of ill distribution by bringing to the disinherited a part of their privileges." Dr. Norman Hoover, Mayo Clinic (AMA Volunteer to Vietnam) and Dr. Ernest B. Howard, Assistant Executive Vice President, AMA, talked and gave slides on their volunteer service in Vietnam, which any doctor may do for a period of two months or more. They stressed the importance of it but that most important is the need for us to help educate doctors there instead of bringing them to our medical schools. Our schools cannot train them in the diseases most seen in Vietnam. Also that conditions are so much better here the doctors don't return to their homeland, thus causing what they call "The Brain Drain" of the under-privileged countries.

Mrs. Anthony P. Cipriano, President-Elect

### In Memoriam

Mrs. E. Roland Hill, of Mystic, Connecticut, who was the thirteenth Connecticut State Auxiliary President in 1956-57.

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# Letter To The Editor

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## To The Editor:

We wish to bring to the attention of Connecticut physicians a recent series of cases of viral hepatitis. The epidemiologic findings may be of state-wide significance. In the New Haven area during the period of August through October there have occurred at least twelve cases of viral hepatitis associated with the illegal parenteral administration of narcotic, barbiturate or amphetamine type drugs among older teenagers and young adults. We believe the observation of jaundice in this age group should serve to raise the index of suspicion of illicit drug use by the patient regardless of his social position or that of his parents. Interrogation of some of the patients suggests that the use of these drugs particularly on a sporadic, intermittent and experimental basis, is sufficiently common and interlinked among young people of differing location and background that additional cases may reasonably be expected not only in the New Haven area but elsewhere.

Several of the recent cases seen by us appear to be infectious hepatitis. In such instances gamma globulin prophylaxis of contacts could be expected to be effective in limiting further morbidity and possibly in interrupting the chain of transmission. Vigorous and confidential questioning of viral hepatitis patients is necessary in order to identify likely sources of infection and those contacts who might be in the incubation period.

Viral hepatitis cases associated with drug use tend to exhibit certain characteristic epidemiologic features. Rosenstein<sup>1</sup>, in describing a similar outbreak which occurred in Providence, Rhode Island during 1964-65, noted that 23 of 25 cases occurred in males. The age range was 17-32 yrs. with an average of 21-22 yrs. In the current New Haven group 11 of 12 cases have occurred in males. The age range was 17-21 yrs. with an average of 19-20 yrs. Some of the patients are unemployed high school and college dropouts; others are regularly employed in skilled and semiskilled work; still others are full-time students. In Providence as well as New Haven, Negroes have represented a minority of cases. True addicts are also in the minority. Most patients use drugs only occasionally and exhibit neither scarred arm veins nor drug withdrawal symptoms. This may explain why only 40 per cent of the Providence cases were recognized as drug users by the physician who made the initial diagnosis of hepatitis.

Analysis of recent Connecticut hepatitis morbidity data shows that 100 cases of viral hepatitis have been reported as occurring during the period August 1-October 31. In the age

group 15-29 years there have been 34 cases in males and 8 cases in females. Survey of available case records reveals that parenteral transmission appears possible in at least half of this group. These data, admittedly incomplete, suggests that drug abuse, with the concomitant sharing of contaminated injection equipment, is perhaps currently one of the more common modes of spread of viral hepatitis within this state, particularly among young adult males.

Robert W. McCollum, M.D. Barbara Christine, M.D.  
Earl B. Byrne, M.D. James C. Hart, M.D.  
Department of Epidemiology & Public Health Preventable Diseases Division  
Yale University School of Medicine Connecticut State Department of Health

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<sup>1</sup> Rosenstein, B. J., *J.A.M.A.* (in press).

## Milk Intolerance Among Negroes

Many more Negroes than whites apparently suffer ill effects from drinking milk.

In some adults—about 70 per cent of whom are Negro—milk causes abdominal bloating, cramps, and diarrhea, says a report in the current *Journal of the American Medical Association*.

The victims often have a deficiency of intestinal lactase activity, and therefore are unable to digest the milk sugar, lactose, said the report by two physicians at the Johns Hopkins University School of Medicine, Baltimore.

When the physicians tested 20 white and 20 Negro men volunteers at the Maryland House of Correction, they found 21 who could not tolerate milk. Nineteen of these were Negro.

Earlier studies agree with these findings, and a new report the authors received from Uganda indicates 72 per cent of Negroes there have a lactase deficiency. "The similarity to the 70 per cent incidence in Baltimore is striking," they said.

The cause of this deficiency and its incidence aren't known. It may be hereditary, the result of intestinal injury, or an adaptation to decreased milk-drinking in adulthood.

Assuming for the moment that the deficiency is hereditary, the authors make an interesting observation: milk-drinking after weaning is rare in west-central Africa, the ancestral home of many American Negroes.

Diseases carried by the Tsetse fly make dairy-cattle raising virtually impossible in this section of Africa.

"It is therefore probable," the authors said, "that the ancestors of the Negro drank very little milk and thus had less need for intestinal lactase after infancy. Over many generations, this diminished need might have produced the genetic adjustments which result in the milk intolerance of many Negroes today."

*Letters to the Editor are welcome and will be published for informative and educational purposes as space permits. As with other material which is submitted for publication, all letters will be subject to the usual editing. Address all correspondence to: THE EDITOR, CONNECTICUT MEDICINE, 160 St. Ronan Street, New Haven, Connecticut, 06511.*

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# Laboratory Medicine

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## "Pap" Smears

Routine cytologic examination of cervical-vaginal smears for cancer has proven to be one of the most valuable tests ever employed for the detection of significant disease in an early stage. In the 20 years it has been employed in this state we have gained considerable experience with the problems involved in the technique. Some of these are discussed below.

### Fixation

Traut and Papanicolaou<sup>1</sup> recommended immediate fixation in equal parts of 95 per cent alcohol and ether without permitting drying. This is still the reference method although it has certain drawbacks. The ether-alcohol is volatile, odoriferous and bulky, with attendant problems in transportation and handling the slides. Many laboratories have found that 95 per cent alcohol, appropriately denatured, is cheaper, easier to handle and also effective. Recently Bonime<sup>2</sup> has claimed that air-dried smears are equally satisfactory. After receipt in the laboratory the smears are rehydrated in glycerin-water and are alleged to be of a quality equal to those handled by older techniques. The convenience of this method was so appealing that we tried it for over 1000 patients at the Norwalk Hospital. The results were interesting but discouraging. Apparently good smears can be made in this fashion by some physicians from some patients. All too frequently, however, the smears were of such poor quality that they could not be interpreted. This necessitated the usual cycle of a call to the physician's office, a recall of the patient, involved explanation and reassurance, etc. We therefore abandoned the air-dried smear and do not recommend it for routine use.

A simple and satisfactory substitute for ether-alcohol is the spray fixative which is squirted on the slide immediately after the secretions are smeared. Good results have been obtained with Adams Spray-Cyte.

### The Combined Smear

For routine use the cervical scraping is the best source of material. It does overlook certain cases of endometrial cancer which exfoliate primarily into the vaginal pool. Thus two smears are often submitted for completeness. This involves additional work for the physician and particularly for the cytotechnologist, and increases the cost of the procedure. A method combining the merits of the two-sample technique with the economy of a single

slide for examination has been recommended by Frost<sup>3</sup> as the "Fast combined smear."

After the speculum is inserted (without lubricant) a drop of vaginal pool material is obtained from the posterior fornix and placed one inch from the end of the slide. It is *not* smeared. A cervical scraping from the complete squamocolumnar junction is then obtained at once and mixed with the vaginal pool. Then the gloved fifth finger is used as a spreader and is drawn quickly across the combined drop twice, both times to the far end of the slide. Fixative is immediately sprayed on.

### Frequency of Examination

When "first" smears are made from adult women about 1 in 200 yield significantly abnormal results. "Repeat" smears yield only 1 in 2000 important abnormalities if the first smear was not atypical. Although repetition of pelvic examination and smear every 3 months or 6 months is feasible one may question the potential value of such frequent examination, particularly because the natural history of uterine carcinoma is one of a very slow evolution.

It is well worth considering this problem from the point of view of the cytotechnologist. First, there is a significant shortage of well trained cytotechnologists in Connecticut today. Federal grants to the Approved Schools in the state and to the trainees should help alleviate this shortage in a year or two. Second and more important because it will exist no matter how many technologists are employed, is the factor of boredom with subsequent inattention. A good "screener" can examine 15 to 50 smears a day for cancer. This means that about once in 4 days a fast screener can expect to find a positive slide in her own material if she is looking at "first" smears. For "repeats" she may see nothing but negatives for 40 working days (8 weeks) if she is speedy, or 133 working days (26 weeks!) if she is slow. To cut down this problem of inattention it is incumbent on attending physicians to limit the number of repeat smears to the fewest which will safeguard the patient. A routine smear a year is probably entirely adequate for patients whose first smear is not abnormal.

ROY N. BARNETT, M.D.

### References

1. Papanicolaou, G. N. Traut, H. F., and Marchetti, A. A.: *The Epithelia of Woman's Reproductive Organs*. New York, Commonwealth Fund, 1948.
2. Bonime, R. G.: "Air-dried smear for cytologic studies"; *Obs. and Gyn.* 27, 783-790, June 1966.
3. Frost, John K.; loc cit.



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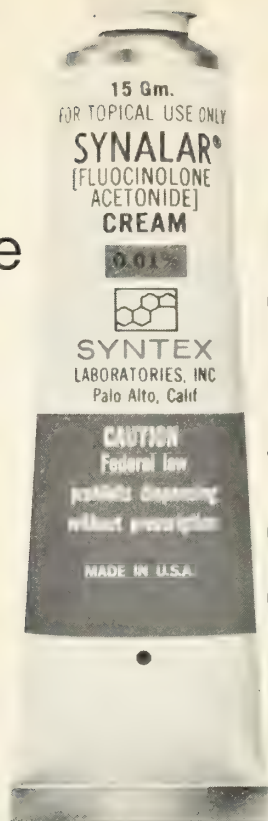
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have an adverse effect on pregnancy, the safety of their use on pregnant females has not absolutely been established. Therefore, they should not be used extensively on pregnant patients, in large amounts, or for prolonged periods of time. 2. *Occlusive dressing method*—With occlusion of extensive areas, systemic absorption of the corticosteroid may occur, and suitable precautions should be taken. Occasional patients may show contact sensitivity to a particular dressing material or adhesive. Miliaria, folliculitis, pyoderma have been seen infrequently with the use of this technique. 3. *Development of infection* requires appropriate antibacterial therapy and continuation of the occlusive dressing method. Local atrophy and striae have been reported with protracted occlusive dressing therapy. While relapses can be expected to occur in many psoriatic patients, remission may persist for several weeks to several months in favorable cases. 4. *Patient whose psoriasis is in an active stage, with recent appearance of new lesions, may not be a good candidate and may show early relapse.* So plastic films may be flammable, and due care should be exercised in their use. Similarly, caution should be employed when such films are used on left near children to avoid the possibility of accidental suffocation. **Effects:** Side effects are not ordinarily encountered with topically applied corticosteroids. As with all drugs, however, a few patients may react unfavorably to Synalar under certain conditions. **References:** 1. Cahn, M. M., & Levy, E. J.: *J New Drugs* 1:262 (Nov.-Dec.) 1961. 2. Meenan, F. O.: *J Am Med Ass* 52:75 (Mar.) 1963. 3. Robinson, H. M., Jr., Raskin, J., and Dunse W. J. R.: *Southern Med J* 56:797 (Jul.) 1963.



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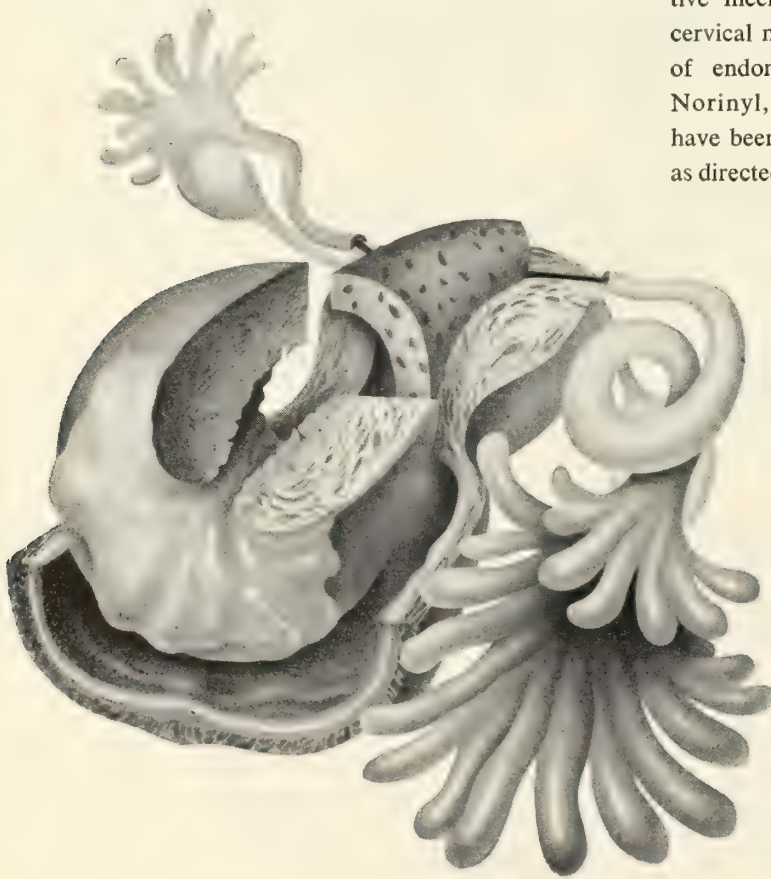
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firm the findings of the Ad Hoc Advisory Committee appointed by the Food and Drug Administration to review this possibility. Cardiac, renal or hepatic dysfunction. Carcinoma of the breast or genital tract. Patients with a history of psychic depression should be carefully studied and the drug discontinued if depression recurs to marked degree. Patients with a history of cerebral vascular accident.

**Warning:** Discontinue medication pending examination if there is sudden partial or complete loss of vision, or if there is a sudden onset of proptosis, diplopia or migraine. If examination reveals papilledema or retinal vascular lesions, medication should be withdrawn.

**Precautions:** By May 1963, experience with norethindrone 2 mg.—mestranol 0.1 mg. had extended over 24 months. Through miscalculation, omission or error in taking the recommended dosage of Norinyl, pregnancy may result. If regular menses fail to appear and treatment schedule has not been adhered to, or if patient misses two menstrual periods, possibility of pregnancy should be resolved before resuming Norinyl. If pregnancy is established, Norinyl should be discontinued during period of gestation since virilization of the female fetus has been reported with oral use of progestational agents or estrogen. When lactation is desired, withhold Norinyl until nursing needs are established. Existing uterine fibroids may increase in size. In metabolic or endocrine disorders, careful clinical preevaluation is indicated. A few patients without evidence of hyperthyroidism had elevated serum protein-bound iodine levels, which in the light of present knowledge, does not necessarily imply hyperthyroidism. Protein-bound iodine increased following estrogen administration. Bromsulphalein retention has occurred in up to 25% of patients without evidence of hepatic dysfunction. Studies from 24-hour urine collections have shown an increase in aldosterone and 17-

ketosteroids and decrease in 17-hydroxycorticoid levels. Thus, Norinyl should be discontinued prior to and during thyroid, liver or adrenal function tests. Because progestational agents may cause fluid retention, conditions such as epilepsy, migraine and asthma require careful observation. Thus far no deleterious effect on pituitary, ovarian or adrenal function has been noted; however, long-range possible effect on these and other organs must await more prolonged observation. Norinyl should be used with caution in patients with bone, renal or any disease involving calcium or phosphorus metabolism. **Side Effects:** Intermenstrual bleeding; amenorrhea; symptoms resembling early pregnancy, such as nausea, breast engorgement or enlargement, chloasma and minor degree of fluid retention (if these should occur and patient has not strictly adhered to medication plan, she should be tested for pregnancy); weight gain; subjective complaints such as headache, dizziness, nervousness, irritability; in a few patients libido was increased. In a total of 3,090 patients, 2.2% discontinued medication because of nausea.

**NOTE:** See sections on contraindications and precautions for possible side effects on other organ systems.

**Dosage and Administration:** One Norinyl tablet orally for 20 days, commencing on day 5 through and including day 24 of the menstrual cycle. (Day 1 is the first day of menstrual bleeding.)

**Availability:** Dispensers of 20 and 60 tablets; bottles of 100.

**References:** 1. Council on Drugs. JAMA 187:664 (Feb. 29) 1964. 2. Brvans, F. E.: Canad Med Ass J 92:287 (Feb. 6) 1965. 3. Goldzieher, J. W.: Med Clin N Amer 48:529 (Mar.) 1964. 4. Cohen, M. R.: Paper presented at Symposium on Low-Dosage Oral Contraception, Palo Alto, Calif., July 15, 1965. Reported in Med Sci 16:26 (Nov.) 1965. 5. Hammond, D. O.: Ibid. 6. Rice-Wray, E., Goldzieher, J. W., and Aranda-Rosell, A.: Fertil Steril 14:402 (Jul.-Aug.) 1963. 7. Goldzieher, J. W., Moses, L. E., and Ellis, L. T.: JAMA 180:359 (May 5) 1962. 8. Kempers, R. D.: GP 29:88 (Jan.) 1964. 9. Tyler, E. T.: JAMA 187:562 (Feb. 22) 1964. 10. Rudel, H. W., Martinez-Manautou, J., and Maqueo-Topete, M.: Fertil Steril 16:158 (Mar.-Apr.) 1965. 11. Flowers, C. E., Jr.: N Carolina Med J 25:139 (Apr.) 1964. 12. Goldzieher, J. W.: Appl Ther 6:503 (June) 1964. 13. The Control of Fertility. Report adopted by the Committee on Human Reproduction of the American Medical Association. JAMA 194:462 (Oct. 25) 1965. 14. Flowers, C. E., Jr.: JAMA 188:1115 (June 29) 1964. 15. Merritt, R. I.: Appl Ther 6:427 (May) 1964. 16. Newland, D. O.: Paper presented at Symposium on Low-Dosage Oral Contraception, Palo Alto, Calif., July 15, 1965. Reported in Med Sci 16:26 (Nov.) 1965.

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# Special Notices

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## NEW ENGLAND POSTGRADUATE ASSEMBLY

January 17-19, 1967

Statler Hilton Hotel Boston, Massachusetts

### Tuesday, January 17

- 8:00 A.M. Film: DNA—"The Story of Life." Discussor: William H. Baker, M.D.
- 9:00 A.M. Panel: "Breast Cancer." Moderator: Oliver Cope, M.D., Boston.  
Panelists: Robert Ravdin, M.D., Philadelphia; Henry Kohn, M.D., Boston; Elinor D. Montague, M.D., Houston; Benjamin Castleman, M.D., Boston
- 10:20 A.M. Panel: "Postgraduate Education." Moderator: George Dunlop, M.D., Boston  
Panelists: Earle Wilkins, M.D., Boston; Daniel D. Federman, M.D., Boston; George Robertson, M.D., Boston; Norman Stearns, M.D., Boston
- 12:30 P.M. Luncheon—Speaker: Bradford Cannon, M.D., Boston  
"Traumatic Surgery of Face and Skin"
- 2:00 P.M. Panel: "Preoperative Medical Examination." Moderator: W. Allan Tisdale, M.D., Burlington, Vermont  
Panelists: Burton S. Tabakin, M.D., "Pulmonary Insufficiency"; George W. Welsh, 3rd, M.D., "Diabetes Mellitus"; Thomas C. Gibson, M.D., "Cardiac Disease"; W. Allan Tisdale, M.D., "Hepatic Disease"; all from Burlington, Vermont.
- 3:20 P.M. "The Pathophysiology of the Alcoholic Neurological Disorders." Kurt Isselbacher, M.D., Boston and Maurice Victor, M.D., Cleveland, Ohio
- 8:00 P.M. "Subversive Activities of the Communists in this Country." Dr. Fern C. Stukenbroeker, F.B.I., Washington, D. C.

### Wednesday, January 18

- 8:00 A.M. Film: "Diagnostic Significance of Venous Pulse."
- 9:00 A.M. Panel: "The Medical & Surgical Aspects of Acquired Valvular Heart Disease." Moderator: W. Gerald Austen, M.D., Boston  
Panelists: Roman DeSanctis, M.D., Boston & Charles Sanders, M.D., Boston
- 10:20 A.M. Panel: "Surgical Treatment of Vascular Disease." Moderator: Michael DeBakey, M.D., Houston  
Panelists: Allan Callow, M.D., Boston; John Mannick, M.D., Boston and Robert Linton, M.D., Boston
- 12:30 P.M. Luncheon: Speaker: Kenneth Bird, M.D., Boston  
"Myco Bacterial Disease: Child and Adult."
- 2:00 P.M. Panel: "Spare Parts and Transplants." Moderator: David Hume, M.D., Richmond, Va.  
Panelists: Anthony P. Monaco, M.D., Boston and Joseph Murray, M.D., Boston

- 3:20 P.M. "President's Program for Stroke, Heart and Cancer Centers." Michael DeBakey, M.D., Houston, Texas
- 8:00 P.M. "Public Relations."  
Speakers: Professional Staff from the AMA, Chicago

### Thursday, January 19

- 8:00 A.M. Film: "Abortion and the Law." Discussor: John Grover, M.D., Boston
- 9:00 A.M. Panel: "Sex Education." Moderator: Thomas J. Boag, M.D., "Sex Problems in Older People."  
Panelists:  
Mary Jane Gray, M.D., "Advice Concerning Sexual Problems, to Adolescents and Young Adults, as seen by an Obstetrician; J. Ward Stackpole, M.D., "How the Pediatrician deals with Sexual Attitudes & Problems in Adolescents"; Victor E. Chase, M.D., "Sexual Attitudes & Problems of the Young Adult; Mental Health Implications", all from Burlington, Vermont
- 11:00 A.M. Panel: "Recognition and Treatment of Mental Retardation."  
Moderator: Mary Louise Scholl, M.D., Boston  
Panelists: Richard L. Naeye, M.D., Burlington, "Intrauterine Undernutrition, a Cause of Mental Retardation"; Mary L. S. Efron, M.D., Boston, "Inborn Metabolic Errors Related to Mental Retardation"; Randolph K. Byers, M.D., Boston, "Intellectual Effects on Mild Encephalopathies"; Murray Sidman, M.D., Boston, "Educational Therapy for the Mentally Retarded Child."
- 12:30 P.M. Luncheon: Speaker: Stephen Goldfinger, M.D., Boston. "The Use of Allopurinol in Gout and Hyperuricemia."
- 2:00 P.M. "The Abortion Problem." John Grover, M.D., Boston.
- 3:00 P.M. "Heart Disease in Infancy." Allan Goldblatt, M.D., Boston.
- 3:30 P.M. "Clinicopathological Conference."

## NEW YORK EYE AND EAR INFIRMARY CLINICAL CONFERENCE

April 10 and 11, 1967

The Annual New York Eye and Ear Infirmary Clinical Conference will be held on April 10 and 11, 1967 in the Biltmore Hotel in New York City.

The Otolaryngology Program will consist of Papers on: "Laryngeal Trauma"; "Laryngeal Stenosis"; "Dysphonia"; "Present Status of Stapedectomy"; "Polytomography and Reconstructive Surgery in Chronic Ear Disease."

All interested otolaryngologists are invited to attend this meeting. For registration and further information write: Jane Stark, Registrar, New York Eye and Ear Infirmary, 218 Second Avenue, New York, New York 10003.

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## NEW BOOKS IN REVIEW

### **HERITABLE DISORDERS OF CONNECTIVE TISSUE.**

**Third Edition. Victor A. McKusick, M.D. The C. V. Mosby Company, St. Louis, Missouri, 1966. 499 pp. with 190 illustrations and two in color. \$18.50.**

Reviewed by: LOUIS H. NAHUM

William Harvey wrote in 1657 "Nature is nowhere accustomed more openly to display her secret mysteries than in cases where she traces her workings apart from the beaten path; nor is there any better way to advance the proper practice of medicine than to give our minds to the discovery of the usual law of nature by careful investigation of cases of rarer forms of disease. For it has been found in almost all things, that what they contain of useful or applicable nature is hardly perceived unless we are deprived of them or they become deranged in some way."

It is this philosophy which underlays this classic. The author has sought for a synthesis of the scattered information about generalized disorders of connective tissue that is inherited and given ample justification for which William Harvey states above that clinical investigation of pathologic states is a legitimate method for studying biology. The hereditary syndromes covered in this book may therefore be considered tools for studying the normal situation, in this case specifically the elucidation of connective tissue.

The clinical researchers reported so scholarly in this book impinges on practically every area in medicine, for connective tissue actually connects the numerous branches of medicine and "without connective tissue, medicine would come to pieces even non-viable pieces just like the cells of the human body."

The book is well illustrated, reports on the clinical behavior of hereditary syndromes, the biology of normal connective tissue, on the numerous syndromes of diseases of connective tissue and finally on the future of the study of heritable disorders of connective tissue. It is a first class reference book for every practitioner and specialist in the medical sciences.

**ATLAS OF HERNIA REPAIR. Carl H. Calman, M.D. The C. V. Mosby Company, St. Louis, Missouri, 1966. 150 pp. Illustrated. \$16.75.**

Reviewed by J. A. FABRO

As implied in the title, the author offers a methodical and systematic synopsis of hernia repair, supplemented by plates illustrating the anatomy and surgical repair.

In spite of the fact that "the literature on hernia is voluminous," he feels that there is need for such a volume because in surgical residency programs, the operation for various types of hernia is "without adequate instruction or supervision." He seeks to remedy this defect.

He wishes also to promote the view that "the surgeon should have at his disposal a thorough knowledge of regional anatomy, appreciation of the physiological result desired, and the intelligence and judgment, in each case, to

utilize most advantageously the tissues available." There can be no disagreement with this goal. But does the "Atlas of Hernia Repair" accomplish it? I wonder.

The book is not directed to the fully trained surgeon. I seriously question whether it provides the depth and critical evaluation basic to and necessary in the education of a resident surgeon learning. For example: he says, "A number of prosthetic materials are available for a prosthetic implant: tantalum mesh, Marlex mesh, Dacron and nylon meshes. The author prefers a soft, rather porous Dacron mesh." Is this adequate instruction? Nor does he numerate specific references from the surgical literature to supplement his statements as he goes along. The reader must scan the 100 or so references at the end of the book for authors and titles he may wish to consult.

The 16 chapters include bits of history, of etiology, diagnosis, and complications of hernias ranging from the common inguinal hernia to diaphragmatic hernias and "rare hernias of the pelvic floor," including drawings of the anatomy and surgical technique. The drawings are in black and white, some borrowed from other sources, such as Watson's Hernia and Nyhers and Harkins' Hernia. It is my impression that while the drawings might be adequate for a gross understanding or impression by a medical school student or recent graduate, they would (or should!) be inadequate for a resident in surgery to use as his only source before embarking on the operations described.

It is difficult for me to see how any author, in the style of a synopsis, condensation, or atlas, can in 150 pages present the subject of all the hernias of the abdominal wall adequately for a surgical resident.

Dr. Calman, formerly Assistant in Clinical Surgery at Washington University School of Medicine, undoubtedly understands the surgery of hernia. If it is true, however, as he states, that there is inadequate instruction or supervision in surgical residency programs in this basic operation of hernia, I am sorry to say that I believe his labor of love fails to fill the void.

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**FUNCTIONS OF THE CORPUS CALLOSUM.** *Ciba Foundation Study Group No. 20. Editor and Organizer: E. G. Ettlinger. Editors for the Ciba Foundation: A. V. S. de Reuck and Ruth Porter. The Little, Brown & Company, Boston, Massachusetts, 1965. 156 pp with 28 illustrations. \$3.75.*

Reviewed by: JOHN P. FLYNN

This volume consists of series of papers by clinicians and research workers engaged in the study of the function of the corpus callosum, and anterior commissure, the pathways connecting the two halves of the forebrain. Earlier clinical studies found that the corpus callosum could be cut without any marked neurological symptom appearing. Recent work indicates that the two hemispheres of the brain are relatively independent of one another when the corpus callosum is cut. This was shown by restricting the sensory input to one hemisphere and cutting the corpus callosum. Under these conditions one side of the brain may learn to discriminate complex patterns. If one now tests for learning in the other hemisphere, there is no evidence that it occurred, even though it can learn by itself. In fact the two sides can learn opposing responses simultaneously. Simpler discriminations, like distinguishing between two lights of different brightness or two lights flickering at different rates are learned simultaneously even with the corpus callosum severed.

Comparable results are found when other senses than vision are studied. Some but not all patients, in whom the corpus callosum is absent, show results similar to those obtained in experimental animals, when appropriate testing procedures are used. There are also some slight indications that at times in such patients one hand doesn't know what the other is doing. The early negative findings are explained in part on the supposition that the tests were not sufficiently refined, the patients had found other ways of coping, and having been epileptics they differed from otherwise normal subjects. While this is a book for the specialists, the intricacies of the experimentation make for interesting reading.

**THE HISTORY OF THE AMERICAN MEDICAL WRITERS' ASSOCIATION.** *Volume I. Harold Swansberg, B.S., M.D. Society for Academic Achievement, Quincy, Illinois, 1965. 111 pp. \$2.50.*

Reviewed by: VICTOR L. SZANTON, M.D.

This is a large paperback volume—a veritable beehive of information and memorabilia of the history of this association.

It goes back to the modest beginnings in 1940 as the Mississippi Valley Medical Editor Association and brings it to its present standing as a national organization.

This volume is a nice scrap book through which to meander while sitting on the velvetten settee. It is more than that, too. It forms one of the basic ten commandments of medical writing. A wider spread of the knowledge of these guide lines would make a little less dreaded Allen Gregg's statement "the man of science appears to be the only person who has something to say, and the only man who does not know how to say it." Also, the sources of medical

journalist training are made known. The University of Missouri and the University of Oklahoma as well as the University of Illinois offer a four year course in medical journalism. For those interested in medical writing this is a recommended browse.

**CURRENT SURGICAL MANAGEMENT III.** *Edited by Edwin H. Ellison, M.D., Stanley R. Friesen, M.D., and John H. Mulholland, M.D. W. B. Saunders Company, Philadelphia and London, 1965. 519 pp. \$11.50.*

Reviewed by: HUGH F. LENA

This is the third volume of a series which presents conflicting views on the management of 30 fairly common surgical problems. The first appeared in 1957 and the second in 1960. Both of these were shorter volumes but were well received. This highly instructive and readable book has been written by 104 authors. These doctors are well selected, experienced, and have strong feelings about their subject.

There is a short introduction by one of the editors before each subject is discussed. He gives some background concerning the nature of the disagreement and attempts to be impartial. The editors point out that there was apparently less controversy and more dogmatism in the early days of surgery when knowledge was so imperfect. It is paradoxical that differences of opinion are often greater when more is learned about a condition. Search for the truth about disease often brings out controversy.

These articles are, on the whole, brief, informative, and well presented. The varying viewpoints are seen side by side. At times there is a fundamental difference in concept of treatment of a condition. This is illustrated by Lampe who emphasizes cobalt radiotherapy for treatment of carcinoma of the mid-esophagus while Adams prefers resection and esophago gastrostomy.

At other times the disagreement is less basic and often a mere choice of technique. Madden presents the case for porta to fundus cholecystectomy while Hoerr prefers the fundus to porta technique. Some differences are more apparent than actual. In Klassen's article on the operative management of severe closed chest injuries he also stresses the importance of restoration of a patent airway, effective ventilation, and adequate blood volume. Worman discusses the conservative management of these injuries but also mentions the need for definitive surgery in some cases.

Some of the subjects presented in the first volume in 1957 are again considered, often with a change in emphasis brought on by new discoveries in the field. The management of duodenal ulcer and esophageal varices are noteworthy examples.

This book would be valuable to the Surgical Resident who is often given one point of view about the management of a surgical condition. It would be equally useful to the practicing surgeon to help him maintain a healthy skepticism in interpreting methods of treatments and results. Surgery, of course, is not an exact science. Panel discussions at surgical meetings are often stimulating and valuable to both the participants and to audiences. This volume fulfills a need and may be recommended to any general surgeon.



# MEDICAL NEWS

## A Diet For Cholesterol Reduction

A diet to reduce cholesterol in the blood and, hopefully, to reduce the risk of heart disease, is reported in the current Journal of the American Medical Association.

It remains a question whether diet modification actually reduces heart disease, says a Journal editorial in the same issue. But those susceptible to coronary heart disease "might be advised to follow such dietary principles" in the hope that heart-disease risk could be reduced, the editorial said.

The diet isn't designed to take off weight. Its purpose is to maintain the regular intake of calories while substituting foods that produce less cholesterol.

The diet's features:

—Daily consumption of animal fat is reduced to no more than 20 grams (approximately the amount in seven to eight ounces of lean, cooked meat) in diets of 2,380 to 3,140 calories. About half this much meat is allowed for daily diets of 1,200 to 1,400 calories.

—Eggs, because of their high cholesterol content, are limited to five or fewer a week.

—The remainder of the diet's fat consists of vegetable oils and their products.

The diet research was done at the Cleveland (Ohio) Clinic, and was supported by the National Heart Institute. Authors of the report are Helen Brown, Ph.D., Marilyn Farrand, M.Sc., and Irvine H. Page, M.D.

Effects of 18-day diets on the blood cholesterol levels of young, healthy persons were studied over a five-year period. Animal foods, including eggs, and the amounts and kinds of margarine, cooking fats, and oils were varied and compared.

A standard diet was developed which gave the maximum cholesterol reduction—an average of 12.3 per cent in seven days and 17.7 per cent in 18 days.

Other test diets contained greater amounts of animal fat, and produced significantly less cholesterol reduction.

The standard diet contained no eggs, but tests showed that one egg eaten daily did not significantly hinder cholesterol reduction, provided total animal fat consumption was kept below a certain level. Two eggs, however, wiped out any gains in cholesterol reduction.

The standard diet must be followed closely to be effective, the authors said. Slight variances in consumption of animal and vegetable fats cut cholesterol reduction almost in half during some tests.

"The value of the diet may be nullified with too much 'lean' meat or smaller amounts of meats too high in fat, too many eggs, too little oil or oils too low in polyunsaturates," the Journal editorial said. "The usual problem is that patients may be following a slightly effective diet rather than a fully effective one."

The standard diet was developed in the kitchens of the Cleveland Clinic, using ordinary household foods. It demonstrates, the authors said, that "fat-controlled diets may consist of customary food products providing a variety of appetizing menus. Success of these diets depends upon the talents of the cook."

## Digitalis—Would FDA Approve It Today?

"... I would hate to be introducing digitalis as a new drug today. Anyone reading the toxicity and side effects would never use it in the present climate. However, digitalis has been with us long enough now that the toxicity and side effects have taken their proper place. They are there, to be sure, but not as prominently as the therapeutic effect.—Robert W. Ballard, M.D., in *Food Drug Cosmetic Law Journal*, (21:31-32), January 1966.

## How To Go To Sleep

Let us all remember that we must not prescribe just the dosage that is given in a book; we must give enough to produce the effect we desire. Also we must not rigidly prescribe a dose every four hours; it is better to tell the nurse to give enough of the medicine to relieve pain, and when the pain returns to give another dose. I learned much pharmacology years ago when I watched a man quickly drink four martinis. He explained that he did not feel anything until he had four. And then I thought of the many times I had wondered why a man like that had to take three or four capsules of a barbiturate before he felt sleepy.—Walter C. Alvarez, M.D., in *Modern Medicine*, (34:106), March 14, 1966.

# Connecticut Medicine

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